Table 1—*Reported Cases of Microthymoma**

Source	Age, yr/Gender	Microthymoma			Associated Disease
		Size, mm	Subtype	Capsule	
Cheuk et al[1]	32/male	7	B1/B2	No	PRCA
Cheuk et al[1]	50/male	5	B2	Yes	MG
Shimosato and Mukai[8]	ND	5	B2	No	ND
Nomori et al[10]	28/female	1.5	B2	Yes	MG
Present case	29/female	3	B2	Yes	MG
Present case	36/female	4	B1	Yes	MG
Present case	69/male	2	B2	Yes	MG

*PRCA = pure red cell aplasia; ND = not described.

eosin (HE)–stained sections (range, 4 to 55 sections) were prepared for microscopic examination. From these, we found three microthymomas in three patients (1.5%); the sizes of the microthymomas were 2 to 4 mm (Table 1). The histologic type of the thymoma was classified according to the World Health Organization (WHO) classification.[3]

Case Reports

Patient 1

A 29-year-old woman with generalized type MG underwent total thymectomy via median sternotomy. Preoperative CT found no tumor in the mediastinum. While there was no gross tumor in the nine sections of the resected tissue specimen, microscopic examination revealed an encapsulated thymoma 3 mm in size in the left lobe (Fig 1). It was composed of several lobes with proliferating plump ovoid cells accompanied by small lymphocytes and was classified as a type B2 thymoma based on the WHO classification.

Patient 2

A 36-year-old woman with generalized type MG underwent total thymectomy via median sternotomy. Preoperative CT found no tumor in the mediastinum. While there was no gross tumor in 10 sections of the resected tissue specimen, microscopic examination revealed a thymoma 4 mm in size surrounded by a distinct fibrous capsule in the left lobe, which was classified as type B1 based on the WHO classification.

Patient 3

A 69-year-old man with ocular-type MG and an encapsulated type B2 thymoma 2.2 × 1.7 cm in size underwent thymothymomectomy via median sternotomy. While there was no other gross tumor in 16 sections of the resected tissue specimen, microscopic examination revealed another type B2 thymoma 2 × 2 mm in size surrounded by a fibrous capsule.

Discussion

The term *microthymoma* was first proposed by Cheuk et al[1] in 2005, and is representative of an entity distinct from a *microscopic thymoma*. While the microthymoma is defined as a microscopic-sized thymoma, microscopic thymoma has been reported to be a discrete tiny epithelial island incidentally found in a thymus and might be more appropriately termed *nodular hyperplasia*.[4–8] As reported in the literature, microscopic thymomas usually range from 0.2 to 0.4 mm in size, and are typically found in 15% of patients with MG and in 4% of autopsy specimens.[5,7] The latest WHO classification[9] stipulates

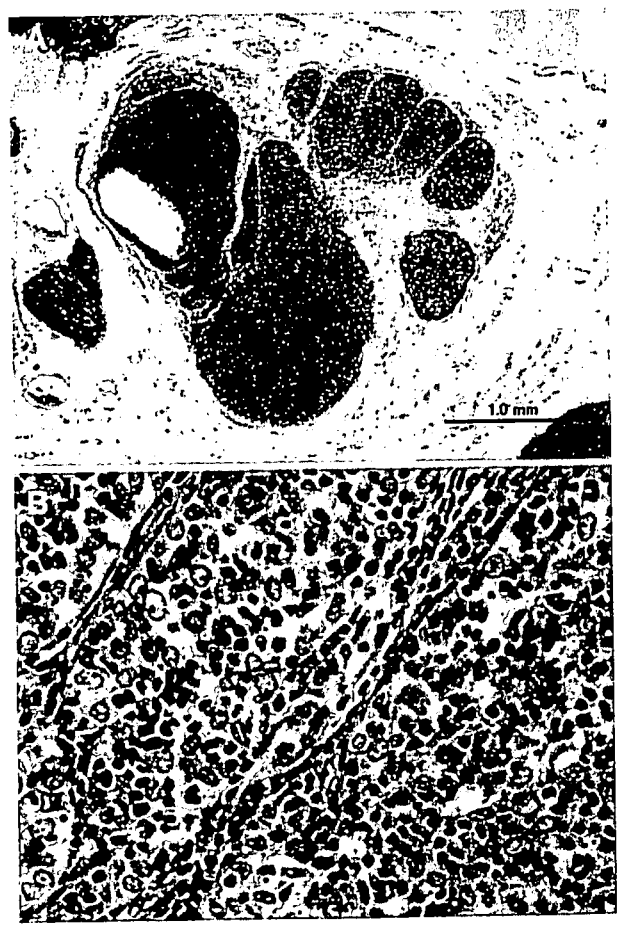

FIGURE 1. *Top, A*: The tumor was 3 mm in diameter and encapsulated by a thick wall (HE, original × 2). *Bottom, B*: The ovoid cells were isolated or formed loose clusters and displayed oval vesicular nuclei and distinct nucleoli (HE, original × 40).

the upper size of limit of microscopic thymoma to be 1 mm. While the conventional thymoma is a discrete mass lesion well demarcated from the adjacent thymic tissue with distinct features, such as lobulation, admixed immature T-cells that are positive for terminal deoxynucleotidyl transferase, and perivascular spaces without medullary differentiation, the microscopic thymoma does not exhibit these features.[1] Therefore, Rosai[2] has suggested renaming microscopic thymomas *nodular hyperplasia* of the thymic epithelium.

From our literature review, there have been seven patients with microthymomas, including our three patients (Table 1).[1,8,10] The mean size of the microthymomas was 4 mm (range, 1.5 to 7 mm). Histologic subtypes were B1 in one patient, B2 in five patients, and B1/B2 in one patient. Five tumors were encapsulated with fibrous tissue, and the other two tumors were nonencapsulated. While the previously reported four microthymomas were incidentally discovered, our three cases were found in approximately 1.5% of 196 patients with MG who underwent thymectomy or thymothymomectomy. Because we examined the resected thymus using an average of 14 HE-stained sections from each patient, microthymoma may be present in approximately 1% of patients with MG. Microthymoma might exist in thymus of patients with MG, even in patients who have no thymoma indicated by CT.

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Three Cases of Multiple Thymoma with a Review of the Literature

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Three cases of patients with synchronous multiple thymoma are reported. Two patients had two thymomas each and the remaining patient had three. The thymomas in each patient all displayed similar histological findings, of which the WHO histological classification were type B2, A and B1, respectively. With a modified Masaoka staging system, the thymomas were determined to be stages II-1 and I in patient 1, one of stage III and two of stage I in patient 2, and two of stage II-1 in patient 3. We reviewed nine reported cases of multiple thymoma in which histological findings were provided and discuss whether they developed from multi-centric origin or from intra-thymic metastasis.

Key words: thymoma – multiple developments – multi-centric development – recurrence

INTRODUCTION

Although it is well known that multiple thymoma can develop in a single patient, its actual incidence is very low. Also it remains controversial whether the cases represent disease of multi-centric origin or intra-thymic metastasis. To address this issue, we present three cases of patients with multiple thymoma and also review the reported cases of which histological findings have been provided (1–8).

MATERIALS AND METHODS

From 1981 to 2005, 96 patients with thymoma were treated by thymo-thymomectomy in the Department of Thoracic Surgery of Kumamoto University Hospital. Of these, three patients (3.1%) had multiple thymomas. The histological type of each thymoma was classified according to the World Health Organization (WHO) classification system (9). The tumor stage was classified by a modified Masaoka classification (10).

CASE REPORT

Patient 1

A 69-year-old male with ocular type myasthenia gravis (MG) was admitted to our hospital for surgical treatment of an anterior mediastinal tumor. The serum level of anti-acethylcholine receptor antibody (AchR Ab) was elevated to 8 nmol/l (normal level < 0.2 nmol/l). Computed tomography (CT) showed a well-defined mass bounded on the ascending aorta (Fig. 1). Thymo-thymomectomy was performed via median sternotomy. While pathological examination diagnosed the tumor as type B2 thymoma 23 × 12 mm in size, pathological examination revealed another type B2 thymoma 2 × 2 mm in size located within the same lobe (Fig. 2). While the intra-operative findings showed no invasion of the main tumor, microscopic invasion into the surrounding thymic tissue was obserbed, i.e. the tumor stage was II-1. The patient is now alive without recurrence of thymoma and with complete remission of MG 5 years after surgery.

Patient 2

A 74-year-old male without MG was admitted to our hospital for surgical treatment of an anterior mediastinal tumor. The serum AchR Ab level was within normal limits. CT revealed a small, ill-defined mass bounding on the ascending aorta (Fig. 3). The intra-operative findings revealed invasion of the tumor into the right middle lobe of the lung and also two additional tumors within the right thymic lobe. A thymo-thymomectomy was performed with wedge resection of the right middle lobe. Pathological diagnosis was type A thymoma in all three of the tumors, the respective sizes were 58 × 35, 24×7 and 10 × 8 mm. The patient was treated with post-operative radiotherapy (50 Gy). He is now alive without recurrence of thymoma 10 months after surgery.

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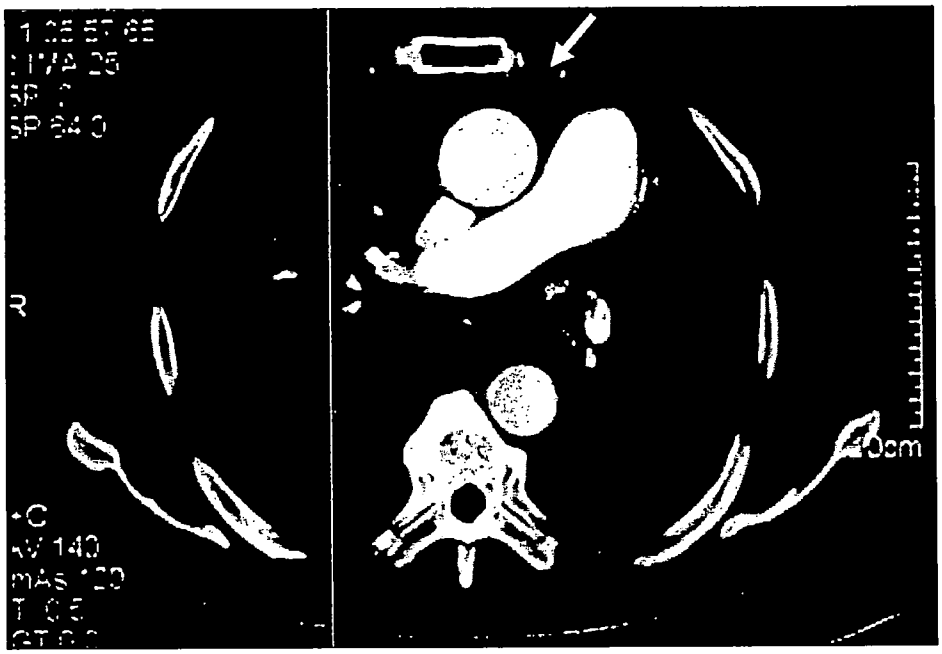

Figure 1. Case 1. Computed tomogram (CT) showing well-defined mass (arrow) bound on the ascending aorta.

PATIENT 3

A 46-year-old male with ocular type MG was admitted to our hospital for surgical treatment of an anterior mediastinal tumor. The serum level of AchR Ab was elevated to 9.5 nmol/l. Computed tomography revealed a well-defined mass on the left upper side of the anterior mediastinum. Thymothymomectomy was performed via median sternotomy. During the operation, another tumor was found within the right lower thymus. The sizes of the two tumors were 22 × 15 and 15 × 8 mm, respectively. Pathological diagnosis was type B1 thymoma in both tumors. While intra-operative findings did not show any invasion by the tumors, pathological examination revealed microscopic invasion into the surrounding thymic tissue in both, i.e. both

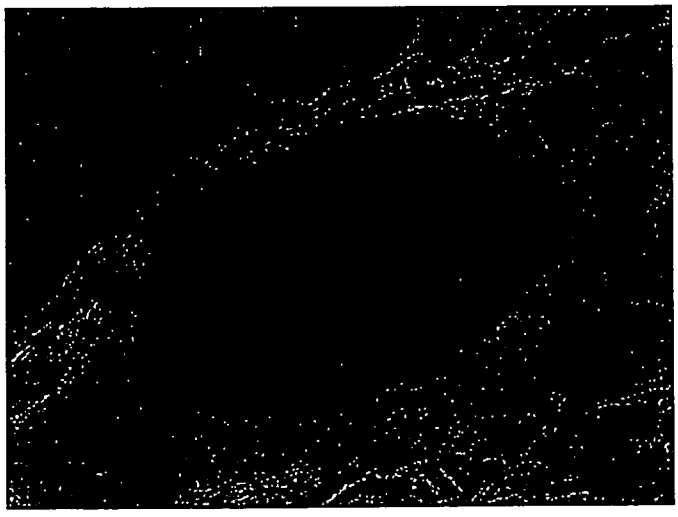

Figure 2. Case 1. A small thymoma existing in the thymic tissue.

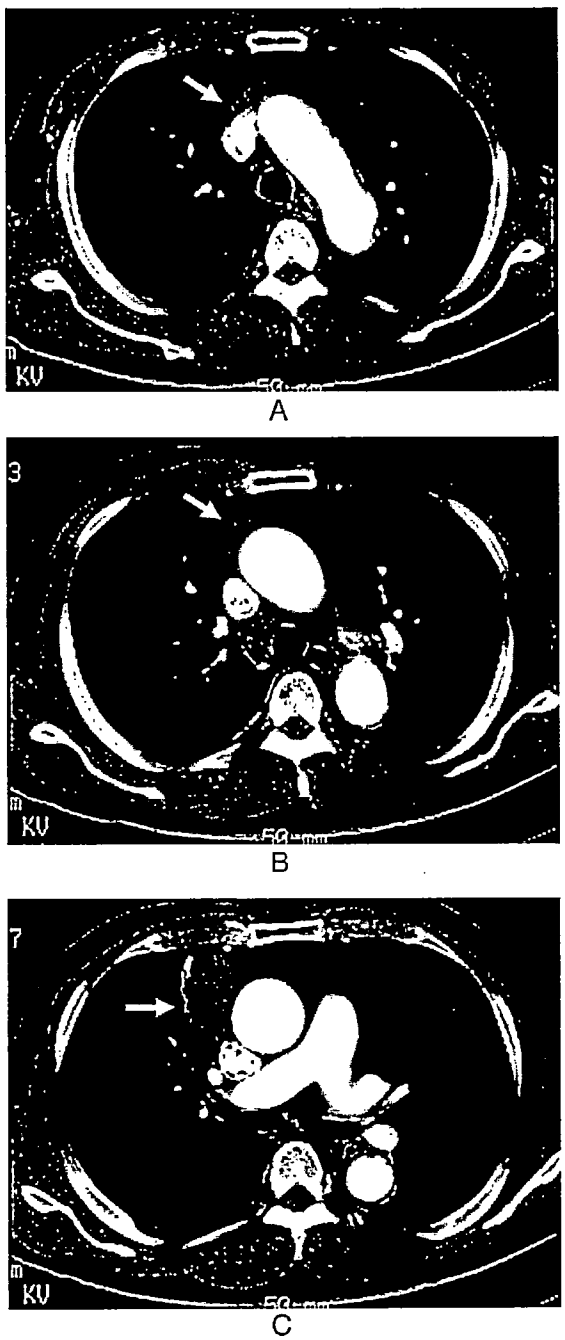

Figure 3. Case 2. CT showing homogenous anterior mediastinal tumor (arrow); one was on the superior vena cava (A), another was on the ascending aorta (B), and last one invaded into the lung (C).

were stage II-1. The patient is now alive without recurrence of thymoma and with complete remission of MG, 6 years after surgery.

DISCUSSION

Multiple thymoma is a well-known phenomenon, but its occurrence is very rare. Bernatz et al. reported just three out of 138 (2.2%) thymomas to be multiple (11). Jaretzky et al. reported one (1.1%) multiple thymoma out of 95 cases of thymoma (12). However, these reports did not describe any histological differences between the multiple thymomas documented. In 1990, Nomori et al. reported one case of multiple thymoma and suggested the possibility of intra-thymic metastasis rather than multi-centric development based on histological, morphometrical and immunohistochemical findings (1). Since their report, nine cases with multiple thymoma have been reported with their histological findings provided (1–8). We reviewed these reports and present their respective clinicopathological characteristics in Table 1. Histological subtypes of thymoma by WHO classification were judged from the histological findings included in each report (9). The characteristics are as follows: (i) mean age was 57 ± 11-year-old (range: 28–81); (ii) there were eight males and four females; (iii) the numbers of thymomas were two in 11 patients, and three in one; (iv) of the total of 25 thymomas, three (12%) could be histologically classified as type A, 13 (52%) as type B1, eight (32%) as type B2, and one (4%) as type B3; (v) histological findings of the multiple thymomas in each patient were similar in 10 patients (83%), while the remaining two (17%) displayed different subtypes; (vi) the difference in tumor size between the thymomas in each patient was such that the smaller ones were usually larger than 25% of the main ones, except for case numbers 1 and 10, which displayed a greater than 10 times size difference between the tumors. Of the 25 thymomas, 20 were stage I (80%), three stage II-1 (12%), and the remaining two were stage III (8%).

It is controversial whether cases of multiple thymomas represent multi-centric origin or intra-thymic metastasis. From the characteristics of the 12 cases in Table 1, multicentric development is suggested by the following characteristics: (i) the number of thymomas were usually less than three, which would be surprising if the source were in intra-thymic dissemination; (ii) there is little size difference between the thymomas in each case, except for case numbers 1 and 10; and (iii) most of the thymomas were stage I, which are essentially unable to spread into the thymic tissue.

However, the possibility of intra-thymic metastasis might be suggested by the finding that each of 10 patients (83%) were found to have similar histological characteristics in their thymomas. While it cannot be concluded at this point whether multiple thymomas are derived from multi-centric development or intra-thymic metastasis, we favor the former hypothesis because of the analysis presented above. While we cannot rule out the theory of intra-thymic metastasis, we believe that most multiple thymomas develop from identical tumor genesis events in each patient, thus resulting in the similar histological findings.

Table 1. Reported cases with multiple thymoma of which histological findings are described

	References/cases	Age/sex	Thymomas		Maximum diameter (mm)	Stage (Modified Masaoka)	Myasthenia gravis
			Number	Histological type*			
1	Nomori et al. 1990 (1)	28/F	2	B2 and B2	70 and 1.5	I and I	+
2	Takeuchi et al. 1997 (2)	74/F	2	B1 and B1	90 and 83	I and I	−
3	Okada et al. 1998 (3)	37/F	2	B1 and B1	55 and 35	I and I	−
4	Okada et al. 1998 (3)	70/M	2	B2 and B2	50 and 24	I and I	−
5	Gotoh and Yokoi 2000 (4)	57/F	2	B1 and B1	39 and 32	I and I	−
6	Hirai et al. 2001 (5)	42/M	2	B1 and B2	40 and 30	I and I	−
7	Ishibashi et al. 2003 (6)	47/M	2	B1 and B1	60 and 25	I and I	+
8	Nonami and Moriki 2004 (7)	81/F	2	B1 and B1	80 and 25	I and I	−
9	Yoneda et al. 2004 (8)	44/M	2	B2 and B3	64 and 60	I and III	−
10	The present cases	69/M	2	B2 and B2	23 and 2	II-1 and I	+
11	The present cases	74/M	3	A, A and A	40, 24 and 10	III, I and I	−
12	The present cases	46/M	2	B1 and B1	22 and 15	II-1 and II-1	+

M, male; F, female.
*WHO classification judged from the histological findings written in each report.

Denzinger et al. reported clonality analysis of multi-focal bladder tumors by examining the loss of heterozygosity (LOH) and fluorescence *in situ* hybridization (FISH) (13). However, it has not been clarified whether these chromosomal losses of primary tumors in epithelial tumors are also preserved in metastatic sites or not. In addition, while Inoue et al. reported the difference of LOH and FISH among histological types of thymoma by using micro-dissection or culture of thymoma-epithelial cells (14), thymoma is generally hard to examine by LOH and FISH owing to many lymphocytes among the thymoma-epithelial cells. Therefore, it is difficult to examine whether the multiple thymomas in our report are from multi-centric origins or metastasis by the clonality analysis, such as the LOH or FISH method.

Finally, it is reported that local recurrence sometimes takes place after resection of non-invasive thymomas (15–17). Maggi et al. reported that two of 133 (1.4%) encapsulated thymomas had recurred after surgery (16). Because these could be recurrences from small or even tiny thymoma remnants in thymic tissue, we recommend an extensive thymectomy even for stage I thymoma.

Conflict of interest statement

None declared.

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less-common causes implicated in its insurgency, and in this light, as suggested by others [3], a chest roentgenogram was performed to rule out a thoracic malignancy. Because thymomas are frequently discovered secondarily to the occurrence of clinical parathymic syndrome, the recognition of an erosive form of OLP as being an autoimmune disease potentially triggered by the presence of a thymoma would be of considerable importance.

In conclusion, although the association between lichen planus and thymoma is rare, the features of our case are in accordance with those previously reported in which an erosive form of OLP could occur, in at least some cases, as a parathymic syndrome. Because the mechanisms that could be implicated have still not been elucidated, it would seem appropriate to suggest that a complete thymoma resection could, in some instances, achieve definitive regression of OLP.

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Successful Steroid Treatment for Fibrosing Mediastinitis and Sclerosing Cervicitis

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The use of steroids to successfully treat a 75-year-old woman with fibrosing mediastinitis and sclerosing cervicitis causing a stricture of the left common carotid artery is reported. Biopsy specimens showed collagenous fibers and fibroblasts with moderate infiltration of lymphocytes. The mediastinal and neck lesions were significantly reduced, with almost complete resolution of arterial stricture, 3 months after initiating administration of prednisolone at 20 mg/d.

(Ann Thorac Surg 2007;83:1199–1201)

It has been reported that steroids, immunosuppressive agents, and tamoxifen have been used in the medical treatment of fibrosing mediastinitis and similar kinds of disorders at other sites [1–4]. Although several reports have showed tamoxifen to be effective, the effectiveness of steroid therapy has been controversial. Here, we present a patient with fibrosing mediastinitis and sclerosing cervicitis causing a stricture of left common carotid artery, who was successfully treated with steroid therapy. A review of the

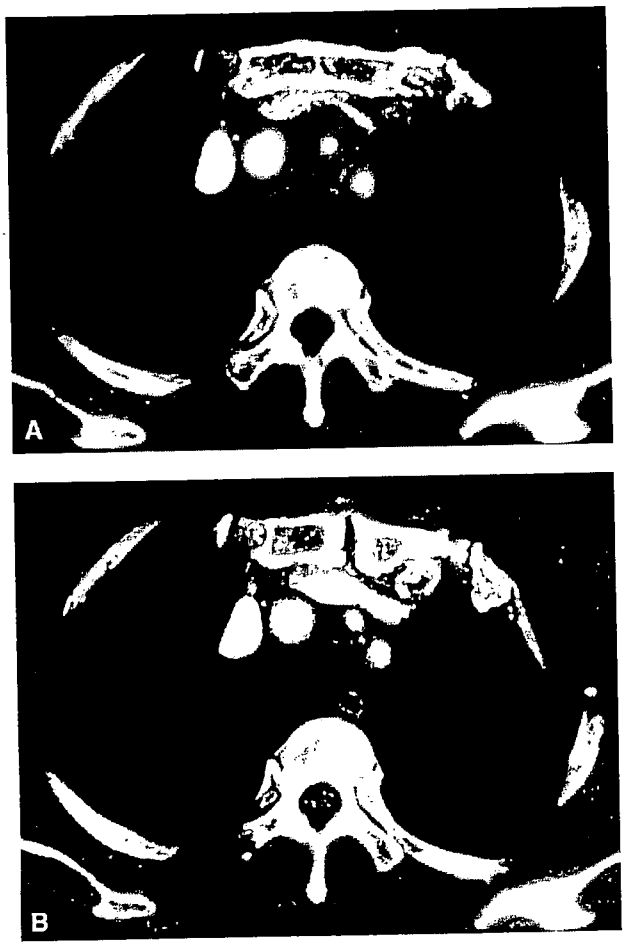

Fig 1. (A) Chest computed tomography at the first medical examination shows the anterior mediastinal mass stricturing the left common carotid artery. (B) After steroid therapy, the mediastinal mass is significantly reduced with almost complete resolution of the stricture of left common carotid artery.

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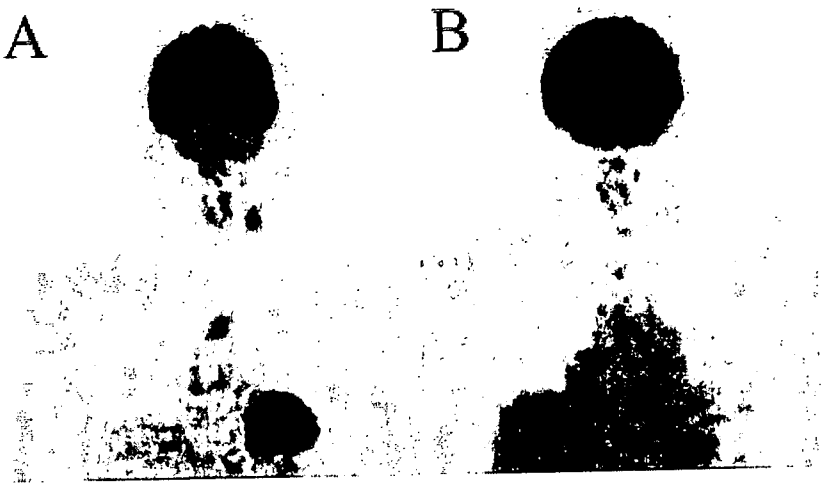

Fig 2. (A) Fluorodeoxyglucose (FDG) positron emission tomography at the first medical examination shows accumulation of FDG at the left neck and mediastinum. (B) After steroid therapy, the prior FDG accumulation at the left neck and mediastinum has disappeared.

English literature shows that this is the second case of the disease successfully treated by steroid therapy alone.

The patient was a 75-year-old woman. In June 2004, she had a right upper lobectomy for pathologic T1N0M0 lung adenocarcinoma when there were no abnormal findings in the mediastinum on computed tomography (CT). In June 2005, she complained of a mass situated at the left upper neck, which was not reduced by antibiotics. There were no other symptoms. A laboratory examination showed no findings of inflammation. A neck CT showed a mass 20 × 18 mm in size around the left common carotid artery. A chest CT also showed a mass 35 × 30 cm in size at the anterior mediastinum above the aortic arch, which caused a conspicuous stricture of the left common carotid artery (Fig 1A). Fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) revealed a high accumulation of FDG at the left neck and the mediastinum (Fig 2A).

A surgical biopsy under general anesthesia showed a lesion firmly adhered to the left common carotid artery. The biopsy specimen showed collagenous fibers and fibroblasts with moderate infiltration of lymphocytes. Both the polymerase chain reaction and histologic stains showed neither fungi nor tuberculosis.

Because of the stricture of the left common carotid artery by the mediastinal lesion, the patient was treated with prednisolone (20 mg/d) after surgery. Three months after the initiation of steroid therapy, CT showed a conspicuous reduction in the size of the mediastinal lesion, with almost complete resolution of stricture of the left common carotid artery (Fig 1B). FDG-PET findings became negative for both the neck and mediastinum (Fig 2B).

Comment

Comings and colleagues [2] originally reported multifocal fibrosclerosis, including 5 disorders consisting of idiopathic fibrosing mediastinitis, Riedel's thyroiditis, idiopathic retroperitoneal fibrosis, sclerosing cholangitis, and pseudotumor of the orbit. A similar disorder occurring in the neck has subsequently been reported and is referred to as sclerosing cervicitis [5]. Symptoms of these disorders are often progressive and cause pain or stricture of the mediastinal vessels and the esophagus. The cause of the disease has been reported to be histoplasma, mycobacterium, *Nocardia*, Hodgkin's disease, sarcoidosis, autoimmune disorders, trauma, and prior surgery, but most cases of the disease are considered to be idiopathic [6].

Our patient had both the fibrosing mediastinitis and sclerosing cervicitis. Although our patient had a history of right upper lobectomy for lung cancer 1 year before the present disease developed, the disease occurred at the anterior mediastinum and the left neck, both of which were completely separate from the site of the prior surgery. We therefore believe that the fibrosing mediastinitis and sclerosing cervicitis in this patient were most probably idiopathic and not caused by the prior surgery.

It has been reported that steroids, immunosuppressive agents, and tamoxifen have been used in the medical treatment of fibrosing mediastinitis and similar kinds of disorders at other sites [1–4]. Several reports have shown tamoxifen to be effective, but the effectiveness of steroid therapy has been controversial. The effectiveness of tamoxifen was first reported by Clark and colleagues [3], who tried this drug in 2 patients with retroperitoneal fibrosis and found dramatic improvement in a small-bowel obstruction and obstructive ureter. Savelli and colleagues [7] reported a young woman with fibrosing mediastinitis and sclerosing cervicitis. She recovered after tamoxifen and steroid treatment, but had a recurrence after cessation of tamoxifen therapy. They therefore concluded that tamoxifen had more significant role in the treatment of the disease than steroids. Bays and colleagues [8] reported 2 patients with fibrosing mediastinitis who were treated with steroids. One patient recovered as a result of steroid-only treatment but the other patient needed tamoxifen as well to bring about an improvement in symptoms [8]. Our patient showed a significant reduction in the mediastinal and neck lesions

with significant resolution of the stricture of the left common carotid artery by steroid therapy alone.

Although there have been several reports of surgical treatment for fibrosing mediastinitis where it caused strictures of the great vessels, esophagus, and airway [9], we believe that idiopathic fibrosing mediastinitis should first be treated by steroids or tamoxifen rather than by surgical treatment if the symptoms do not need immediate relief.

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Bilateral Diaphragmatic Plication in the Setting of Bilateral Sequential Lung Transplantation

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Diaphragmatic paralysis can lead to significant ventilatory impairment, especially if associated with underlying lung disease. Adequate ventilatory mechanics are essential for good outcomes after lung transplantation. We report a case of bilateral diaphragmatic plication at the time of double lung transplantation as an attempt to improve posttransplant ventilation, with good outcome.

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Patients listed for lung transplantation for end-stage lung disease can present with a number of associated abnormalities involving the chest wall, mediastinal structures, and the diaphragm. If possible, correcting any of these problems at the time of transplantation may provide adjuncts for a better recovery in the immediate postoperative course as well as for the long-term outcome.

The patient is a 58-year-old man who had progressive respiratory failure after idiopathic pulmonary lung fibrosis developed 11 years ago. Despite maximal medical therapy, he experienced progressive worsening of symptoms in the form of incapacitating dyspnea and was dependent on home oxygen therapy (3 to 5 L/min) for the last 3 years. That had to be increased to 10 L/min during any form of increased activity, such as walking, and even then, his oxygen saturation would drop to 75%.

During the pretransplantation work-up, spirometry showed a forced vital capacity of 34%, a forced expiratory volume in 1 second of 30%, and a diffusion lung capacity of carbon monoxide of 37%. Compared with a previous study, a chest computed tomography scan showed progression of the underlying parenchymal pathology, with further volume loss bilaterally (but more on the right side), worsening fibrosis, and resultant traction bronchiectasis. Ventilation-perfusion studies showed bilateral reduction that was markedly worse on the right side. These findings were all in keeping with an advanced progressive interstitial lung process.

He was persistently noted to have markedly elevated hemidiaphragms on chest roentgenograms (Fig 1). Fluo-

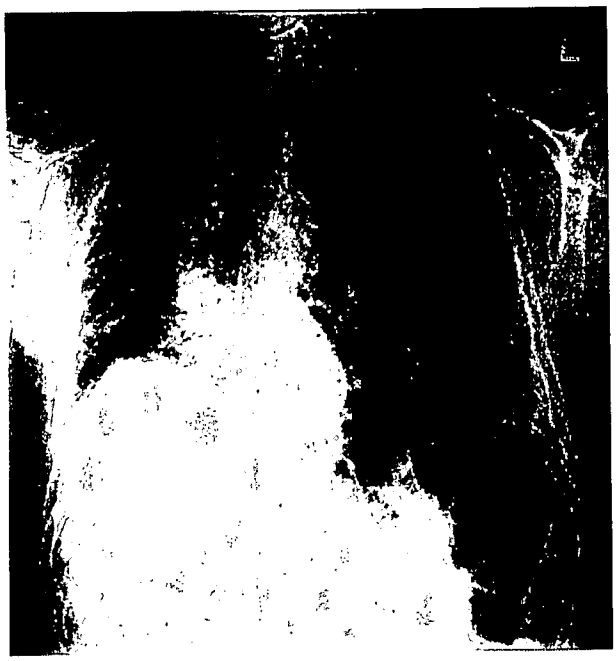

Fig 1. End-stage pulmonary fibrosis with severely elevated hemidiaphragms.

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CHEST Original Research
LUNG PATHOLOGY

Impalpable Pulmonary Nodules With Ground-Glass Opacity*

Success for Making Pathologic Sections With Preoperative Marking by Lipiodol

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Background: **The developments in high-resolution CT scanning have increased the chance of detecting small bronchioloalveolar carcinoma (BAC) or atypical adenomatous hyperplasia (AAH) that appears as a ground-glass opacity (GGO). However, these lesions are not only difficult to localize during surgery, but they are also hard to make pathologic sections of because they are usually impalpable. Here, we report a method of making pathologic sections for impalpable GGO lesions.**

Methods: **Twenty-nine impalpable GGO lesions < 1 cm in size were marked by 0.4 to 0.5 mL of lipiodol under CT scan before surgery. The lesions were resected under C-arm fluoroscopy. The radiopaque areas marked by lipiodol within the formalin-fixed specimens were cut serially under conventional fluoroscopy for pathologic examinations.**

Results: **The mean (± SD) size of the lesions was 0.5 ± 0.2 cm (range, 0.2 to 1 cm), and the mean depth from the pleural surface was 1.6 ± 1.4 cm (range, 0.2 to 6 cm). The mean number of sections submitted for pathologic examinations was 2.3 ± 1.7 per lesion (range, 1 to 7 per lesion). While 11 of the 29 lesions (38%) were invisible even on the cut surface of the specimens, all were demonstrated in hematoxylin-eosin sections. The pathologic diagnosis was BAC in 17 lesions, AAH in 10 lesions, and organized pneumonia in 2 lesions. The use of lipiodol did not affect the pathologic findings.**

Conclusions: **The use of fluoroscopy to cut sections from resected specimens after preoperative marking with lipiodol was useful for making pathologic sections of impalpable GGOs < 1 cm in size.** ***(CHEST 2007; 131:502–506)***

Key words: lung cancer; pathology lung cancer; thoracic surgery

Abbreviations: AAH = atypical adenomatous hyperplasia; BAC = bronchioloalveolar carcinoma; GGO = ground-glass opacity

The development of high-resolution CT scanning has allowed the frequent detection of small ground-glass opacity (GGO) lesions in the lung. Because a percutaneous or transbronchial biopsy of such lesions is often difficult, thoracoscopic surgical techniques have been used in diagnostic excisional biopsies as well as in therapeutic resections. Because small GGO lesions cannot usually be palpated or

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visualized during surgery, several marking techniques have been reported for localization during thoracoscopic surgery, such as those using a dye,[1–3] colored collagen,[4] barium,[5,6] lipiodol,[7,8] microcoil,[9] and hook wire.[10,11] However, even if the lesions are successfully resected, it is still difficult to make pathologic sections of small GGO lesions because they usually cannot be palpated in the resected specimens. In addition, small bronchioloalveolar carcinoma (BAC) and atypical adenomatous hyperplasia (AAH) are sometimes hard to visualize on the cut surface of the resected specimens. This requires many pathologic sections to be made, which is time-consuming and expensive. To resolve these issues, we have performed preoperative marking with lipiodol for impalpable GGO lesions and have made pathologic sections under fluoroscopy, enabling the pathologic diagnosis to be made in all cases. Here, we report on the technique and the results of using it in detail.

Materials and Methods

Eligibility

The CT scan-guided lipiodol marking was approved by the ethics committee of Kumamoto University Hospital in April 2005. Written informed consent was obtained from all patients after they had discussed the risks and benefits of the procedure with the surgeons. Nodules that were potentially difficult to localize during surgery, or difficult to see or palpate on the cut surface of the resected specimens, such as GGO lesions or small nodules situated at a considerable depth from the pleural surface, were candidates for the procedure.

Patients

The nodules that were thought to be difficult to localize under thoracoscopy, such as GGO lesions, nodules situated at a considerable depth from the pleural surface, and nodules < 1 cm in size, were candidates for lipiodol marking. Between May 2005 and June 2006, preoperative lipiodol marking was performed under fluoroscopic CT scanning (AREX-T2310R1; Toshiba; Tokyo, Japan) on 60 nodules in 43 patients. Of these, 29 nodules in 18 patients were impalpable even in the specimens from patients who had undergone resection, who served as subjects in the present study (Table 1). All of the nodules were incidentally detected on CT scan and had no solid component on multidirection CT scans (BRILLIANCE 64; Philips; Amsterdam, the Netherlands), which usually scanned the lesions with 0.5 to 1 mm thickness. All of the nodules were clearly visible, round GGOs < 1 cm in size, which were suspicious for BAC. Of the 29 lesions, 14 accompanied other resectable non-small cell lung cancers, 9 were part of multiple GGOs < 1 cm in size, and the remaining 6 were single GGOs. The mean (± SD) size of the lesions was 0.5 ± 0.2 cm (range, 0.2 to 1 cm), and their mean distance from the pleural surface was 1.6 ± 1.4 cm (range, 0.2 to 6 cm).

Marking Technique

The procedure used for marking was as follows: lesions were usually marked 1 day before surgery under fluoroscopic CT scanning (AREX-T2310R1; Toshiba). Patients were placed on the CT scan table in a suitable position (*ie*, supine or prone). After administering local anesthesia to the thoracic wall, 0.4 to 0.5 mL of lipiodol (Lipiodol Ultrafluid; Laboratorie Guerbet; Aulnay-Sons-Bois, France), which is generally used as a contrast medium for lymphatic vessels, was injected into the nodules under fluoroscopic CT scan guidance (Fig 1).

Table 1—*Clinicopathologic Characteristics of Impalpable Pure GGO Nodules < 1 cm in Size

Characteristics	Values
Size, cm	0.5 ± 0.2 (0.2–1)
Distance from visceral pleura, cm	1.6 ± 1.4 (0.2–6)
Accompanied lesions	
Lung cancer	14
Multiple GGO lesions	9
None (single GGO)	6
Location	
Right upper	9
Right middle	0
Right lower	5
Left upper	7
Left lower	8
Operative procedure	
Wedge resection	23
Segmentectomy	6
Total	29

*Values are given as mean ± SD (range) or No.

Resection Technique

For resection of the marked nodules, a C-arm-shaped fluoroscopic unit was used to detect the radiopaque nodules, which were grasped using a ring-shaped forceps under fluoroscopy in multiple projections. For the deeply situated nodules, segmentectomy was performed. Successful resection of the nodule was finally confirmed by viewing the radiopaque nodule within the resected specimen under C-arm fluoroscopy.

Making the Cut Surface of the Resected Specimen

The resected specimens were inflated and fixed with a syringe of formalin using a thin needle. Intraoperative diagnoses of frozen specimens were not conducted. Formalin-fixed specimens were then viewed under fluoroscopy. The radiopaque area marked by lipiodol was cut serially at 5-mm intervals under fluoroscopy (Fig 2). The sections including the radiopaque area were submitted for pathologic examinations (Fig 3).

Results

All of the nodules could be marked on the CT scan images before surgery. Pneumothorax occurred in seven patients (39%), two of whom (11%) required drainage. No other complications were associated with the lipiodol marking. All of the 29 nodules could be successfully localized during surgery and completely resected. The surgical procedures used were wedge resection for 23 nodules and segmentectomy for 6 nodules.

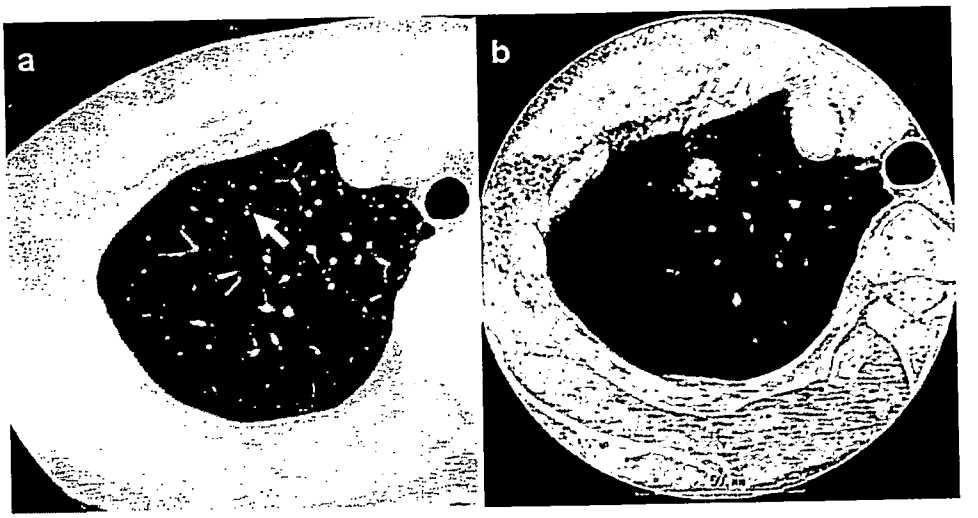

FIGURE 1. *Left, a*: GGO lesion 7 mm in size in the right apical segment (indicated by an arrow). *Right, b*: the lesion is marked with lipiodol.

All of the radiopaque nodules within the resected specimens could be seen distinctly on fluoroscopy even after formalin fixation. The mean number of sections submitted for pathologic examination was 2.3 ± 1.7 sections per lesion (range, 1 to 7 sections per lesion). While 11 of the 29 nodules (38%) could not be seen macroscopically on the cut surface of the sections, all could be seen microscopically and diagnosed pathologically (Table 2).

Pathologic diagnosis was BAC in 17 nodules, AAH in 10, and organized pneumonia in 2. Lipiodol did not affect the pathologic findings. Of the 17 BAC lesions, 6 accompanied the other lung cancers, 7 were part of multiple BAC or AAH lesions, and 4 were single lesions. Of the 10 AAH lesions, 5 accompanied the other lung cancers, and the other 5 were part of multiple BAC or AAH lesions. Of the two lesions with organized pneumonia, one accompanied another lung cancer and the other one accompanied a BAC lesion.

FIGURE 2. Serially cut sections including radiopaque area marked by lipiodol.

DISCUSSION

While the lipiodol-marking procedure is useful for localizing and resecting small pulmonary nodules,[7] it is still difficult to make pathologic sections that include the pulmonary nodules from the resected specimens. This is made particularly difficult by the fact that GGOs < 1 cm in size are generally impalpable. In addition, AAH and BAC lesions < 1 cm in size remain hard to visualize on the cut surface of sections, even after formalin fixation. This requires many pathologic sections to be made, which is time-consuming and expensive. However, the present method enables pathologic sections to be made that include impalpable GGO lesions, which could not only reduce the number of pathologic sections required but also could allow a definitive pathologic diagnosis.

While many small GGO lesions have been found recently by high-resolution CT scans, the management of such lesions remains controversial.[12,13] Small GGO lesions are generally observed initially by CT scanning. Even if a nodule is subsequently discovered to be a BAC, this approach would not miss the chance of surgical cure because it would remain within the T1N0M0 stage during the follow-up period until it grew to 2 cm in size.[14–16] However, for GGOs with CT scan findings that are highly suspicious for BAC, such as those that are round and dense, it would be desirable to perform a surgical biopsy rather than a follow-up for the following reasons: (1) follow-up for at least several years would be necessary because of the slow growth of BAC lesions,[17] which not only causes patients psychological stress but also entails the expense of follow-up CT scans; (2) while BAC lesions < 2 cm in size could

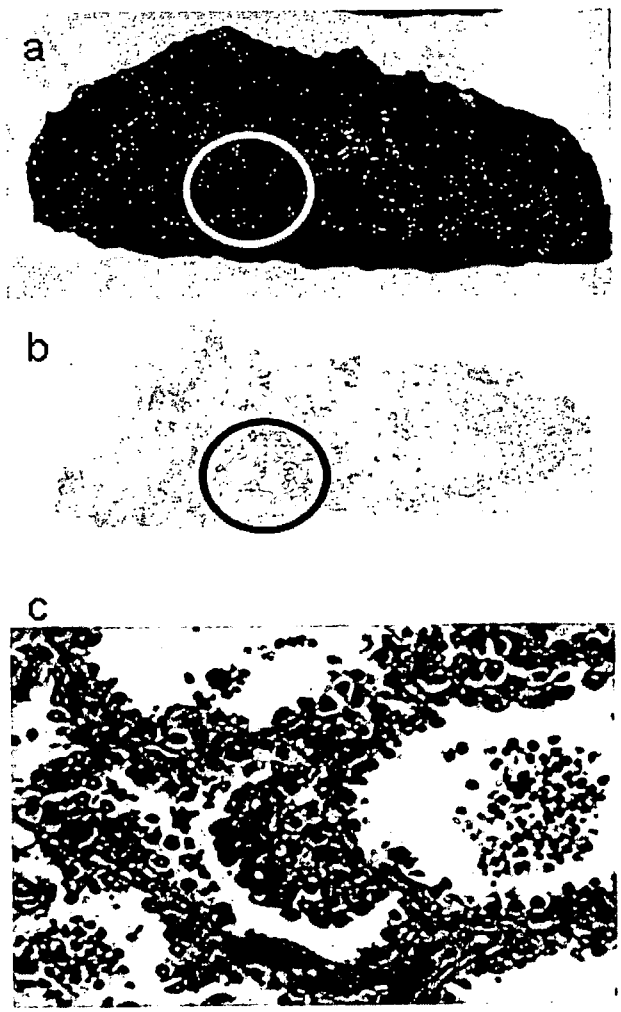

FIGURE 3. *Top, a*: the cut surface of the radiopaque area (indicated by a circle), where the lesion cannot be seen. *Middle, b*: the hematoxylin-eosin-stained section of the same section (the lesion is indicated by a circle). *Bottom, c*: the microscopic findings of the hematoxylin-eosin-stained section (×100), which is histologically diagnosed as BAC.

be cured by limited lung resection, follow-up might result in tumors increasing in size and becoming more aggressive. This could miss the chance of a cure by limited resection and increase the need for lobectomy.[18,19] In addition, CT scan examinations before surgery for general lung cancers sometimes detect other small GGOs, and it is then necessary to understand whether these are double lung cancers or intrapulmonary metastases. Of the 29 GGO lesions in the present study, 17 were BAC lesions and 12 were nonmalignant lesions, including 10 AAH lesions. The 17 lesions with BAC could be cured by limited resection. Of the 12 nonmalignant lesions, 6 were resected with their associated lung cancers, which enabled accurate TNM staging. The remaining six nonmalignant lesions were resected along with their associated BAC or AAH lesion < 1 cm in size; in this latter scenario, pathologic diagnosis could be made and follow-up could be discontinued for a considerable time. We therefore think that a positive surgical biopsy finding is acceptable for GGO lesions with CT scan findings that are highly suspicious of BAC or is accompanied by other lung cancers, even if those were < 1 cm in size.

Table 2—*Macroscopic Findings and Pathologic Diagnosis of the Nodules*

Pathologic Diagnosis	Macroscopic Finding		Total
	Visible	Nonvisible	
BAC	10	7	17
AAH	7	3	10
Organizing pneumonia	1	1	2
Total	18	11	29

Several marking methods have been reported for the localization of small pulmonary nodules. These include the hook-wire technique,[10,11] microcoil,[9] barium marking via bronchoscopy or percutaneous injection,[5,6] percutaneous injections of dyes,[1–3] colored collagen,[4] and lipiodol.[7,8] Because the general dye substances are water soluble, it is impossible to localize the dye-marked lesions after formalin fixation. The microcoil is under phase I study and has not been available in routine use.[9] The barium is seen as a lesion in the hematoxylin-eosin-stained sections and also causes an inflammatory change of the lung tissue, which might make a pathologic diagnosis difficult. The hook-wire technique has been reported to cause massive air embolism,[20,21] which had led to its prohibition in Japan. The lipiodol that was used in the present study not only stays at an injected site even after formalin fixation due to its insolubility in water but also never affects the pathologic findings of the injected site. We therefore think that lipiodol could be one of the optimal markers for not only localizing GGO lesions but also making pathologic sections from resected specimens.

The only complication of lipiodol marking in the present study was pneumothorax in seven patients (39%), two of whom (11%) required drainage. This arose due to the insertion of the needle into the lung but not due to the lipiodol itself. Although we have never encountered air embolisms during percutaneous needle insertion into the lung, the risk of this complication has been reported to be 0.02 to 0.07%.[20] In addition, lipiodol itself poses a potential risk of embolism because it is insoluble in water. We therefore take the following precautions: (1) prior to the injection of lipiodol, the syringe is withdrawn to confirm that blood has not flowed backward; (2) a

minimum amount of lipiodol, up to 0.5 mL, is injected; and (3) lipiodol is injected under fluoroscopic CT scanning to confirm that it does not enter vessels during injection. While there have been no reports of embolism due to lipiodol itself, patients should be informed of the potential risk. Moreover, the procedure should be performed with an awareness of the risk of embolism due to air or lipiodol.

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GTS

The distribution of parenchyma, follicles, and lymphocyte subsets in thymus of patients with myasthenia gravis, with special reference to remission after thymectomy

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Drs Ikeda, Mori, and Nomori (*left to right*). The bronze statue is Dr Shibasaburo Kitasato.

Objective: We sought to examine the distribution of parenchyma, follicles, and lymphocyte subsets in the thymus of patients with myasthenia gravis and to identify determinants of remission after thymectomy.

Methods: Sixty patients with myasthenia gravis who underwent thymectomy were examined. The thymus was divided into upper, middle, and lower parts. The upper part was defined as the superior horn, the lower part as the inferior horn, and the middle part as tissue located between the 2 horns. The percentage of parenchyma was measured morphometrically. The degree of follicular hyperplasia was classified into 5 grades. The densities of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes were classified into 5 grades. The remission of myasthenia gravis after thymectomy was examined with those variables in each part of the thymus.

Results: The middle part had the highest percentage of parenchyma, the highest grade of follicular hyperplasia, and the highest density of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes among the 3 parts ($P < .001$-$.05$). The grades of follicular hyperplasia in the middle and lower parts were significantly higher in patients with improvement of myasthenia gravis than in those without ($P < .05$). The densities of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes in the cortex of the middle part were significantly higher in patients with improvement than in those without improvement ($P < .01$-$.05$).

Conclusions: The thymus has a heterogeneous distribution of parenchyma, follicles, and lymphocyte subsets. The middle part had the largest parenchyma, the highest grade of follicular hyperplasia, and the highest densities of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes among the 3 parts of the thymus. The grade of follicular hyperplasia and the density of these lymphocyte subsets are predictive of improvement in myasthenia gravis after thymectomy.

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The grade of follicular hyperplasia (FH) in the thymus has been reported to be a significant factor for predicting remission of myasthenia gravis (MG) after thymectomy.[1-4] However, it has not been determined whether the distribution of parenchyma and follicles is uniform in the thymus. If these distributions are not uniform, the part of the thymus that is most appropriate for predicting remission of MG after thymectomy requires clarification. To examine these issues, we studied the following: (1) the thymus was divided into the upper, middle, and lower parts; (2) the percentage of parenchyma, grade of FH, and density of lymphocyte subsets in each part were investigated; and (3) the relationship between those variables and the remission of MG after thymectomy was analyzed.

Materials and Methods

One hundred six consecutive patients with MG were treated with extended thymectomy from 1997 through 2004 at the Department of Thoracic Surgery of Kumamoto University Hospital.

GTS

Abbreviations and Acronyms
FH = follicular hyperplasia
MG = myasthenia gravis

Of the 106 patients, 60 were available for pathological examination of the upper, middle, and lower parts of the thymus (Table 1). We studied these 60 patients retrospectively. All 60 patients had an extended thymectomy or extended thymothymomectomy through a median sternotomy.

The thymus was divided into 3 parts (ie, upper, middle, and lower; Figure 1). The upper part of the thymus was defined as the bilateral superior horns. The lower part was defined as the bilateral inferior horns. The middle part was defined as the tissue between the upper and lower parts. After fixation with formalin, these 3 pieces were usually sliced at intervals of 10 mm, resulting in an average of 16 tissue blocks (range, 5-55) submitted for pathological examination in each patient.

The percentage of parenchyma in each part of the thymus was measured by using the following method: (1) a hematoxylin and eosin–stained section was viewed under a macro lens and was displayed on the screen of a 3CCD digital color camera-computer system (FX380, Olympus Co); (2) the image of the whole of the selected section was outlined with a mouse on the screen, including both the parenchyma and adipose tissue, and the data were processed by using a computer, which calculated the total area; (3) the area of parenchyma was likewise calculated; and (4) the percentage of parenchyma was derived from the area of parenchyma divided by the total area.

The degree of FH of the thymus was classified into 5 grades according to the classification of the MG study group of the Ministry of Health and Welfare of Japan in 1977: grade 0, involuted thymus; grade I, accumulation of lymphocytes in the distended medulla; grade II, 1 follicle in 1 section; grade III, 2 to 4 follicles in 1 section; and grade IV, more than 5 follicles in 1 section or more than 1 follicle in each lobule.

An immunohistochemical analysis of lymphocytes using markers for CD3, CD4, and CD8 (Nichirei Co) was performed in each part. The density of lymphocyte subsets stained with these markers was classified into 5 grades: grade 0, no positive cells; grade I, scattered positive cells, grade II, fewer than half positive cells; grade III, more than half positive cells; and grade IV, almost all lymphocytes positive.

TABLE 1. Patient characteristics

Male/female sex	16/44
Mean age, range (y)	51 ± 18 (13–80)
Grade of MG (Osserman)	
I	6
II	32
III	20
IV	2
Thymoma/nonthymoma	19/41
Outcome of operation	
A	10
B	40
C	9
D	0
E	1

MG, Myasthenia gravis.

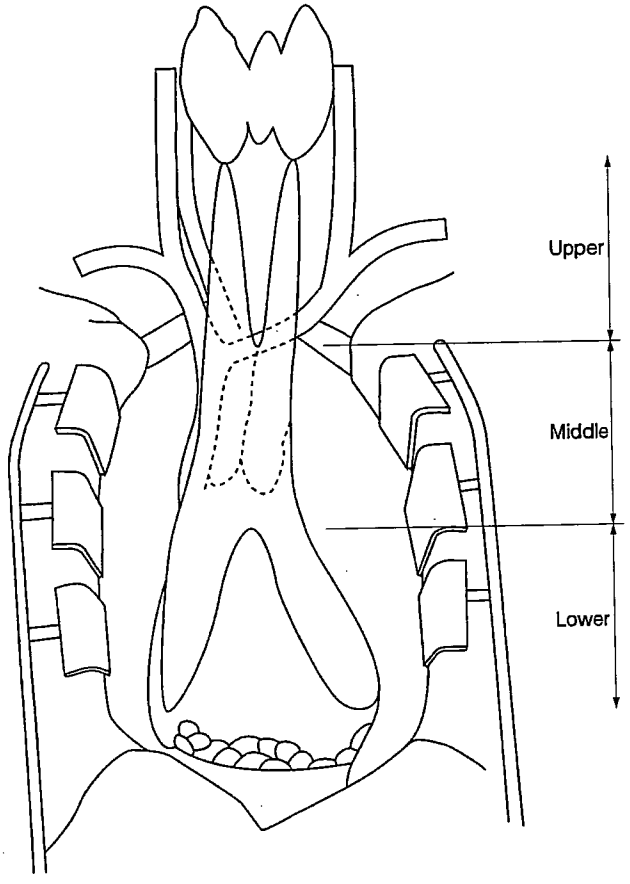

Figure 1. Definition of upper, middle, and lower parts of the thymus in the present study.

The postoperative outcome was obtained from hospital records or by means of telephone contact with a validated questionnaire. The investigation was approved by the institutional committee in 2005. The outcome of MG after thymectomy was classified from A to E: A, no symptoms and without medication; B, improvement and reduction in medication; C, no change; D, symptoms worse; and E, death caused by MG.

Differences in the percentage of parenchyma among parts of the thymus were analyzed by using paired Student *t* tests. Differences in the grade of FH and density of lymphocyte subsets in each part of the thymus were analyzed by using Wilcoxon signed-rank tests. Differences in the percentage of parenchyma between patients with and without improvement after thymectomy were analyzed with *t* tests. Differences in the grade of FH and the density of lymphocyte subsets between the patients with improvement and those without improvement were analyzed by using Mann–Whitney *U* tests. The Bonferroni test was used to determine

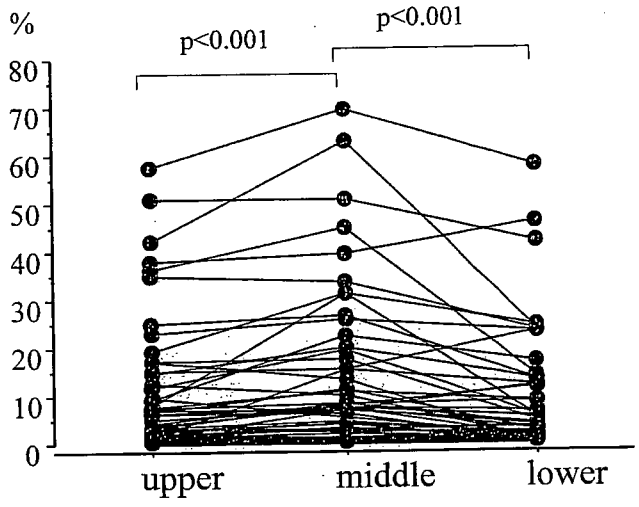

Figure 2. Percentage of parenchyma in each part of the thymus.

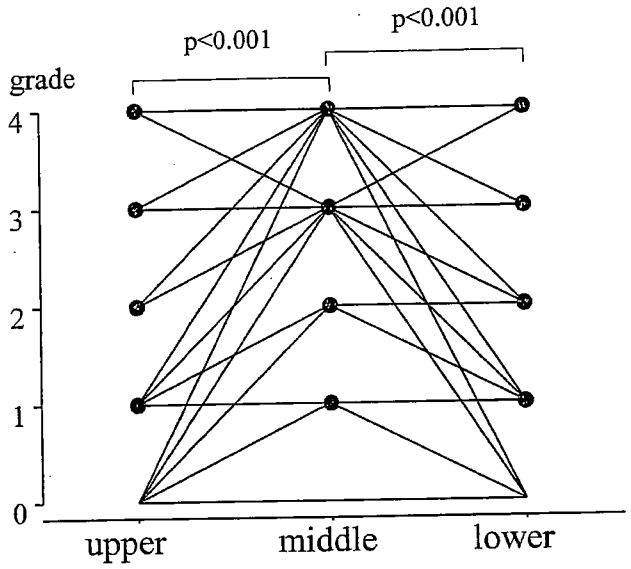

Figure 3. Grades of follicular hyperplasia in each part of the thymus.

significance for comparisons among the 3 parts. All values in the text and tables are presented as means ± standard deviation.

Results

The average of the total area of the upper, middle, and lower parts of the thymus was 4.2 ± 3.3, 7.6 ± 4.3, and 5.8 ± 4.3 cm^2, respectively. The average area of parenchyma was 0.3 ± 0.5, 0.8 ± 1.2, and 0.4 ± 0.7 cm^2 in the upper, middle, and lower parts of the thymus, respectively. As a result, the average percentage of parenchyma was 9.2% ± 13.1%, 11.8% ± 15.7%, and 7.5% ± 12.0% in the upper, middle, and lower parts of the thymus, respectively (Figure 2). The percentage of parenchyma in the middle part of the thymus was significantly greater than in either the upper or lower parts ($P < .001$).

The average grade of FH was 1.6 ± 1.5, 2.7 ± 1.7, and 1.4 ± 1.6 in the upper, middle, and lower parts of the thymus, respectively (Figure 3). The grade in the middle part was significantly higher than in the upper or lower parts ($P < .001$).

The distributions of densities of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes in the cortex and medulla of each part of the thymus are summarized in Table 2. Although the density of $CD3^+$ lymphocytes was significantly higher in the medulla than in the cortex of each part ($P < .0001$), the densities of $CD4^+$ and $CD8^+$ lymphocytes were significantly higher in the cortex than in the medulla of each part ($P < .0001$). In the cortex the densities of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes were significantly higher in the middle part than in the upper or lower parts ($P < .001$-.05), except for difference in density of $CD3^+$ lymphocytes between the upper and middle parts. In the medulla the densities of $CD4^+$ lymphocytes were significantly higher in the middle part than in the lower parts ($P < .05$).

The mean follow-up period after thymectomy was 49 ± 28 months. A postoperative status of A was seen in 10 patients, B in 40 patients, C in 9 patients, and E in 1 patient. The patient with a postoperative status of E was a 79-year-old woman who died of a myasthenic crisis 49 months after thymectomy. Figure 4 shows the percentage of parenchyma of each part of the thymus in 50 patients with improvement (A and B) and 10 patients without improvement (C, D, and E), showing no significant difference between the 2 groups ($P = .16$, .09, and .12, respectively).

Figure 5 shows the grades of FH of each part of the thymus in patients with and without improvement. Although the grade of FH in the middle and lower parts was significantly higher in patients with improvement than in

TABLE 2. Distribution of density of lymphocyte subsets in the thymus

	Density of lymphocyte subsets		
	$CD3^+$	$CD4^+$	$CD8^+$
Cortex			
Upper	1.5 ± 0.8	1.6 ± 0.9†	2.0 ± 0.8†
Middle	1.5 ± 0.7*	2.1 ± 1.0†	2.4 ± 0.8†
Lower	1.2 ± 0.8*	1.6 ± 1.1†	2.0 ± 1.1*
Medulla			
Upper	1.9 ± 0.6	1.2 ± 0.8	0.8 ± 0.5
Middle	2.0 ± 0.7	1.3 ± 0.7*	0.9 ± 0.5
Lower	1.8 ± 0.9	1.1 ± 0.8*	0.8 ± 0.5

Upper, Upper part of the thymus; *Middle*, middle part of the thymus; *Lower*, lower part of the thymus. *$P < .05$; †$P < .01$; ‡$P < .001$.

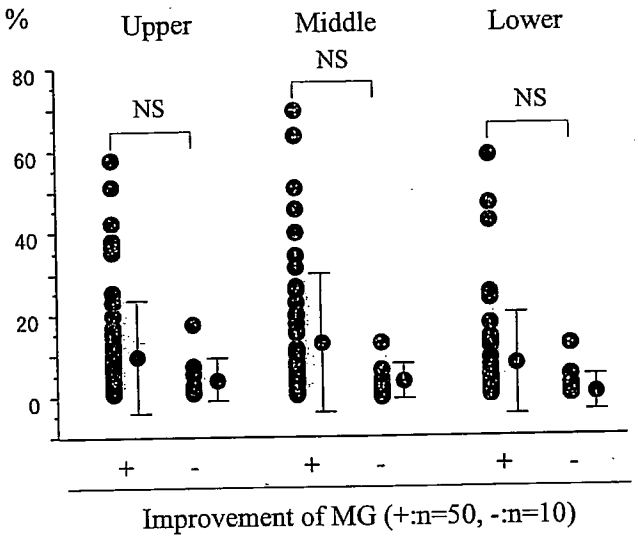

Figure 4. Differences in percentage of parenchyma in each part of the thymus between patients with and without improvement of myasthenia gravis after thymectomy. *NS*, Nonsignificant; *MG*, myasthenia gravis.

those without (P = .026 and .044, respectively), that in the upper part did not show a significant difference (P = .16).

The densities of $CD3^+$, $CD4^+$ and $CD8^+$ lymphocytes in the cortex and medulla of each part of the thymus in patients with improvement and in those without are summarized in

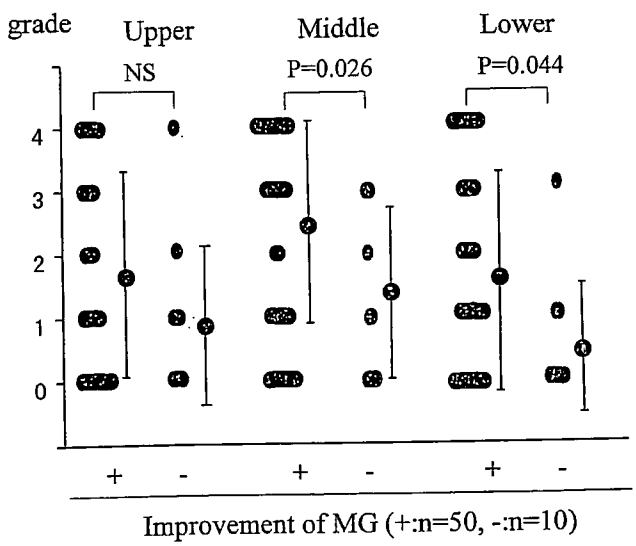

Figure 5. Differences in grade of follicular hyperplasia in each part of the thymus between patients with and without improvement of myasthenia gravis after thymectomy. *NS*, Nonsignificant; *MG*, myasthenia gravis.

TABLE 3. Density of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes in each part of the thymus in patients with and without improvement of myasthenia gravis after thymectomy

	Improvement of MG (+/−)		
	Density of:		
	$CD3^+$	$CD4^+$	$CD8^+$
Cortex			
Upper	1.6/0.9*	1.8/0.9†	2.1/1.7
Middle	1.6/0.9†	2.2/1.4*	2.5/1.7*
Lower	1.8/1.1	1.7/1.0	2.1/1.8
Medulla			
Upper	2.0/1.5*	1.3/0.8	0.8/0.6
Middle	2.1/1.6	1.4/0.7†	0.9/0.7
Lower	1.8/1.5	1.1/0.7	0.8/0.7

Upper, Upper part of the thymus; *Middle*, middle part of the thymus; *Lower*, lower part of the thymus. *$P < .05$, †$P < .01$.

Table 3. The results in the cortex were as follows: (1) although the densities of $CD3^+$ lymphocytes in the upper and middle parts were higher in patients with improvement than in those without (P = .012 and .003, respectively), the difference in the lower part was not significant (P = .8); (2) although the densities of $CD4^+$ lymphocytes in the upper and middle parts were higher in patients with improvement than in those without (P = .006 and .015, respectively), the difference in the lower part was not significant (P = .8); and (3) although the density of $CD8^+$ lymphocytes in the middle part was higher in the patients with improvement than in those without improvement (P = .014), the differences in the upper and lower parts were not significant (P = .1 and .4, respectively). In the medulla (1) the density of $CD3^+$ lymphocytes in the upper part was higher in patients with improvement than in those without (P = .012), but the differences in the middle and lower parts were not significant (P = .054 and .3, respectively); (2) the density of $CD4^+$ lymphocytes in the middle part was higher in patients with improvement than in those without (P = .007), but the differences in the upper and lower parts were not significant (P = .07 and .13, respectively); and (3) the density of $CD8^+$ lymphocytes did not show significant differences between patients with improvement and those without in any of the 3 parts (P = .2, .2, and .7, respectively). Thus the differences in density of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes between patients with improvement and those without improvement were most significant in the cortex of the middle part of the thymus.

Pathological differences of thymus (eg, thymic hyperplasia, involuted thymus, and thymoma) did not affect the above results.

Discussion

The present study revealed 3 main points: (1) the middle part of the thymus had the highest percentage of paren-

chyma, the highest grade of FH, and the highest densities of lymphocyte subsets of the 3 parts; (2) the grades of FH in the middle and lower parts showed significant correlations with remission of MG after thymectomy, although that in the upper part did not; and (3) the densities of $CD3^+$, $CD4^+$ and $CD8^+$ lymphocytes in the cortex of the middle part showed the greatest correlation with remission of MG after thymectomy, whereas those in the other parts showed less correlation.

The distribution of parenchyma, follicles, and lymphocyte subsets in the thymus has not been previously reported. The present study examined the differences of the percentage of parenchyma, grade of FH, and densities of $CD3^+$, $CD4^+$, and $CD8^+$ lymphocytes in the upper, middle, and lower parts of the thymus and revealed that the middle part had significantly higher values of these variables than the other parts. Therefore we conclude that the middle part of the thymus is the most representative area for examining parenchyma, follicles, and lymphocyte subsets.

It has been reported that patients with MG with FH of the thymus have higher remission rates after thymectomy than those without,[1-4] but other authors have disputed this.[5,6] The present study showed that the grades of FH in the middle and lower parts of the thymus were higher in patients with improvement than in those without improvement, although the grades in the upper part did not show a significant difference. Therefore to predict the outcome after thymectomy from the grade of FH, the middle or lower part is more appropriate than the upper part.

The present study has shown that the thymus has a heterogeneous distribution of parenchyma, follicles, and T-cell subsets. The middle part had the largest parenchyma, the highest grade of FH, and the highest density of T-cell subsets. Both the grade of FH and density of T-cell subsets in the middle part had significant correlation with improvement of MG after thymectomy. The middle part of the thymus is therefore the most representative area not only for histopathological examination but also for predicting improvement of MG after thymectomy.

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Original Article

The Efficacy of Epidural Analgesia after Video-Assisted Thoracoscopic Surgery: A Randomized Control Study

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Purpose: Video-assisted thoracoscopic surgery (VATS) is known to reduce the severity of pain after surgery. However, it has not yet been established whether epidural anesthesia/analgesia (EA) is necessary after VATS. We therefore conducted a randomized control study to examine whether or not EA is necessary for pain control after VATS.

Patients and Methods: Forty-six patients undergoing VATS were randomly allocated to one of 2 groups: 24 who were given EA after the procedure (EA group) and 22 who were not (NEA group). Patients in the EA group received a continuous infusion of fentanyl and bupivacaine via an epidural catheter for 2 days after VATS. The degree of postoperative pain was assessed on the total dose of additional analgesics administered, a visual analog scale (VAS), a verbal pain score at rest (VPS-R) and on movement (VPS-M), from the day of surgery to the 2nd postoperative day (2 POD).

Results: Additional use of rectal diclofenac sodium and intramuscular pentazocine was more frequent in the NEA group than in the EA group ($p<0.05$). The VAS, VPS-R, and VPS-M scores were significantly lower in the EA group than in the NEA group at 0 POD, from 0 to 1 POD, and from 0 to 2 POD, respectively ($p<0.0001$–0.05). Stepwise regression analysis revealed that EA was a significant independent variable of VPS-R and VPS-M from 0 to 1 POD ($p<0.05$). However, the incidence of nausea/vomiting in the EA group was 29%, which was more frequent than in the NEA group (5%) ($p<0.05$).

Conclusion: While EA causes nausea/vomiting in some patients, it is effective for pain control until 1 POD after VATS, especially for pain on movements. (Ann Thorac Cardiovasc Surg 2006; 12: 313–8)

Key words: epidural anesthesia, video-assisted thoracoscopic surgery, pain control

Introduction

The application of video-assisted surgery has not only provided the benefit of minimal invasion but has also revolutionized operative procedures and postoperative management. Video-assisted thoracoscopic surgery (VATS) requires only a small skin incision and no rib retraction. This causes minimal damage to the thoracic wall, resulting in a decrease in postoperative pain, postoperative pulmonary dysfunction, and postoperative morbidity and mortality.[1–6] The application of VATS has led to a change in postoperative management, especially in pain control.[7,8]

There is no precise data on how many patients receive epidural anesthesia/analgesia (EA) following thoracic surgery. In 2004, Wu et al. reported the effect of postop-

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