**Table 2.** Components of tumor cells observed in pathological and cytological specimens

| Case | Methods | Component of tumor cells in pathological specimens | | | | Component of tumor cells in cytological specimens | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | spindle cells | giant cells | AD | LA | spindle cells | giant cells | AD | LA |
| 1 | TI | present | present | present | present | X | present | present | present |
| 2 | TI | present | present | present | present | X | present | present | present |
| 4 | Cr | present | | present | | X | | present | |
| 7 | TI | present | present | present | | present | present | X | |
| 8 | TI | present | | present | | present | | present | |
| 9 | Br | present | present | | | present | present | | |
| 10 | Br | present | present | present | | present | present | X | |
| 12 | Br | | present | | | | present | | |

AD = Adenocarcinoma; Br = brushing; Cr = curettage; LA = large-cell carcinoma; TI = touch imprint; X = absent.

**Table 3.** Summary of cytological features of sarcomatoid component of pleomorphic carcinoma and giant cell carcinoma

| | | | |
|---|---|---|---|
| Background | necrosis | present | 2/8 (25%) |
| | type of cells | lymphocytes, neutrophils | 7/8 (88%) |
| Amount of tumor cells | | large | 5/8 (63%) |
| Clusters | size | small | 4/8 (50%) |
| | nuclear overlapping | not obvious | 8/8 (100%) |
| | arrangement | 2-dimensional | 6/8 (75%) |
| Cells | shape | spindle, pleomorphic, variable | 8/8 (100%) |
| | size | large | 7/8 (88%) |
| | variability in size | 5 times or more | 4/8 (50%) |
| | pleomorphism | marked | 7/8 (88%) |
| | margin | demarcated | 5/8 (63%) |
| | cell adhesion | poor | 7/8 (88%) |
| Cytoplasm | color | green/blue | 8/8 (100%) |
| | nature | translucent or vacuole, thick | 8/8 (100%) |
| Nucleocytoplasmic ratio | | increased | 7/8 (88%) |
| Nucleus | location | centrifugal | 5/8 (63%) |
| | shape | irregular, oval | 8/8 (100%) |
| | size | 5 times of lymphocyte or more | 4/8 (50%) |
| | variability in size | 5 times or more | 4/8 (50%) |
| | nuclear membrane | thin, slightly thick | 8/8 (100%) |
| | hyperchromatism | present | 8/8 (100%) |
| | chromatin texture | coarsely granular | 7/8 (88%) |
| | distribution of chromatin | uneven | 5/8 (63%) |
| Nucleolus | shape | round | 7/8 (88%) |
| | size | medium | 4/8 (50%) |
| | number | single | 7/8 (88%) |

ily from the glass slide during the staining process. On the other hand, the adenocarcinoma component was not observed in cytological specimens from cases 7 and 10. Pathological specimens from case 7 revealed that the adenocarcinoma component was a solid adenocarcinoma with mucin that had bizarre nuclei. Giant cells and spindle cells were marked in this case, and mucin in the cytoplasm was difficult to discern in cytological specimens. Pathological specimens in case 10 revealed that the adenocarcioma component comprised a small percentage of the tumor. This may be the reason why the adenocarcinoma component did not appear in cytological specimens from case 10.

There have been only a few cytological studies of GC [12, 13]. GC cytology specimens have exhibited numerous mono- or multinucleate giant cells with significant pleomorphism in size and shape. The cytoplasm of the giant cells is abundant, eosinophilic, microvesicular, and well demarcated. Most of the tumor cells have round, oval or irregularly shaped macronuclei with coarse, granular chromatin and large, prominent nucleoli. Their cytoplasm is occasionally infiltrated with neutrophils. The tumor cells usually occurred singly, and the background contains tumor diathesis with numerous polymorphonuclear leukocytes [12, 13].

Giant cells are one component of PC or GC [1]. However, there is no clear definition of how large these giant cells are. Fishback et al. reported that the single large pleomorphic nucleus of GC measured greater than the diameter of four small resting lymphocytes [14]. Guillan and Zelman reported that the giant cells varied in size from 50 to 120 μm in diameter [15], and Hellstrom and Fisher reported that the giant cells measured from 80 to 100 μm [16]. This vague definition of giant cells causes confusion among pathologists. In our study, the mononucleated giant tumor cells had large nuclei, the size of which was greater than the diameter of 5 resting lymphocytes in half of the cases. There was variability in the size of the nuclei, and the size of the largest nucleus was 5 times greater than that of the smallest nucleus of the tumor cells in half of the cases.

It has been reported that the prognosis for PC patients is worse than that for patients with other NSCLC in surgically resected cases [2–4]. In contrast, Nakajima et al. reported similar clinical behaviors and prognosis between PC and other NSCLC [7]. Pelosi et al. reported that stage I PC behaves more aggressively than ordinary NSCLC; however, the differences were not statistically significant for both overall and disease-free survival curves [6]. Yamamoto et al. reported that the overall 5-year survival rate of surgically resected PC was 80.0% and the disease-free survival rate was 63.3%, which were both far better than rates reported elsewhere [5].

PCs have been reported to be highly metastatic. In our study, some patients had a recurrence even though the tumor was stage I or II; the patient with a stage IA tumor had a recurrence in the lung 31 months after surgery (case 7), and 1 patient with a stage IIB tumor had a brain metastasis 21 months after the surgery (case 8). In contrast, some patients had a favorable prognosis. One patient with a stage IIB tumor is alive 5 years after surgery without any adjuvant therapy (case 9). One patient with a stage IIIA tumor underwent thoracic radiotherapy and chemotherapy (CDDP + GEM) and is alive without recurrence 40 months after the surgery (case 10). One patient (case 12) had an enlarged right adrenal gland the size of which was 15 mm, and its size had become 53 mm six months later. It was surgically removed and confirmed to be metastasis from a pulmonary PC. The patient is alive 23 months after the surgery of the lung tumor.

The contradictory prognoses of PC in different studies may be due to the different criteria of PC used among pathologists. Because ours is a multidisciplinary study, we selected cases that underwent pathological review by pathologists specialized for lung cancers. We did not include patients treated with chemotherapy or radiotherapy before the surgery, because these therapies may modify the tumor cells and enlarge them even further. The present study, by analyzing carefully selected PC or GC cases, suggests that some patients with PC or GC can expect long survival after resection of the tumor with adjuvant therapy. We could not address the pathological or molecular differences between long-survivors and short-survivors suffering from PC or GC. Further studies are needed to clarify the mechanisms of different biological behaviors among this type of lung carcinoma.

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the endocardial linear lesion with the roofline resulted in conversion to sinus rhythm (Figure 1, *B* and *C*).

Bilateral video-assisted thoracoscopic PV isolation is a safe, beating-heart approach for curative surgical treatment of AF.[1] Linear lesions are known to improve the outcome of catheter ablation in patients with persistent atrial fibrillation.[2] The left fibrous trigone line was introduced by Edgerton and colleagues.[3] This linear lesion serves as an alternative to the endocardial mitral isthmus line extending from the left inferior PV to the mitral valve annulus. The creation of a completely transmural left fibrous trigone line can be hampered by the presence of epicardial fat. Not completely transmural lesions exhibit zones of low voltages and conduction slowing and can become pro-arrhythmic.[4] In our patient, an incomplete left fibrous trigone line resulted in left atrial flutter. Most of these iatrogenic arrhythmias are very symptomatic. To prevent, as much as possible, such reentry circuits from occurring, it is of paramount importance to prove complete transmurality of each deployed linear lesion. This can effectively be done using an epicardial approach or a combined simultaneous thoracoscopic surgical and transvenous catheter procedure.[5]

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# Extremely rare but potential complication of diffuse brain edema due to air embolism during lung segmentectomy with selected segmental inflation technique by syringe needle during video-assisted thoracoscopic surgery

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A 65-year-old man was diagnosed with right lung cancer in the upper lobe and S8 segment.

To avoid right pneumonectomy, he underwent right upper lobectomy and S8 segmentectomy by video-assisted thoracoscopic surgery. During segmentectomy, the A8 was ligated first, and then B8 was resected using an automatic stapler. An 18-gauge needle was inserted in the distal B8 bronchus without any blood regurgitation. After removing the inner needle, an air tube of a Bolheal Spray Set (The Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan) with a filter attached was connected to the outer

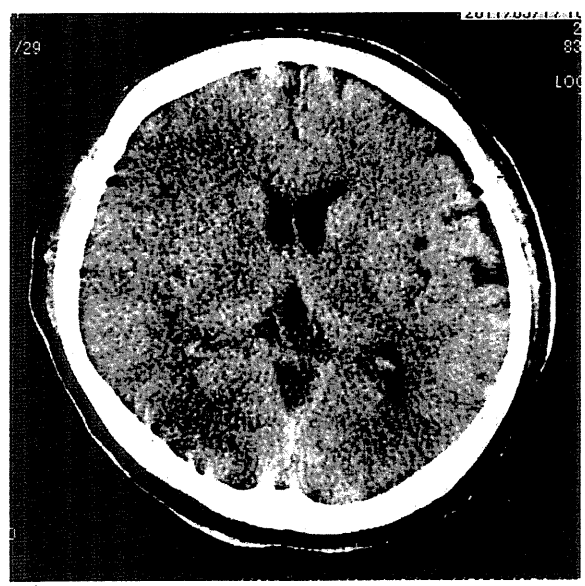

**FIGURE 1.** Computed tomography scan after hyperbaric oxygen therapy revealing diffuse brain edema.

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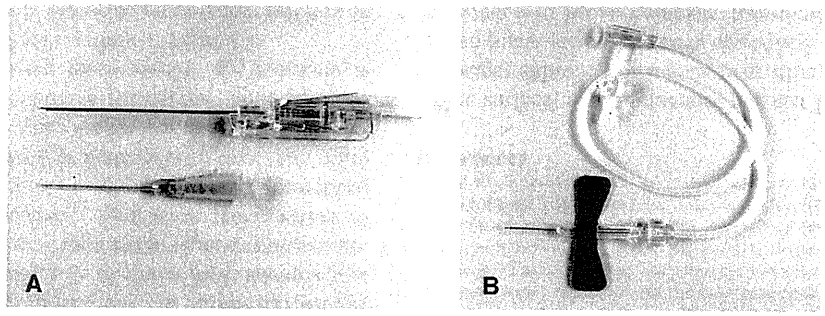


**FIGURE 2.** Needles used during lung segmentectomy with selected segmental inflation technique: A, inner needle *(Upper)* and outer sheath *(Lower)*; B, other type of needle (butterfly needle) used during lung segmentectomy with selected segmental inflation technique.

dwelling sheath, and air was blown into the tube. Because the air was not confirmed in the target area, which usually inflates, we stopped blowing air and removed the punctured in-dwelling needle. Immediately after this, a sudden elevation in blood pressure (220 mm Hg/150 mm Hg) and a decline in end-tidal carbon dioxide pressure were observed, and ST-segment elevation on the electrocardiogram followed. On the transthoracic echocardiogram, air in the right atrium was observed and was diagnosed as an air embolism. Because the bronchus and pulmonary artery of the right S8 were already resected at this point, we decided to continue with the segmentectomy. The bronchial lumen was confirmed, and the sheath without the needle was inserted to blow air into the lumen. Segmentectomy using the automatic stapler was then completed. Immediately after the operation, hyperbaric oxygen therapy was performed. However, computed tomography images showed diffuse brain edema, and cerebral infarction was diagnosed (Figure 1). After 1 week of hypothermic therapy at 35°C, the body temperature was restored, and the respirator was removed 2 weeks after the operation. Although symptoms of left hemiplegia and left spatial neglect were observed immediately after the first hyperbaric oxygen therapy, they were almost completely absent by 4 weeks after the operation.

With progress and the wide use of computed tomography, the number of smaller lesions being detected has been increasing,[1] and segmentectomy with video-assisted thoracoscopic surgery has been one of the common methods. Because of the poor working spaces with video-assisted thoracoscopic surgery, several procedures for detecting the demarcation lines have been reported. Among them, the selected segmental inflation technique is frequently used in Japan.[2,3] Some thoracic surgeons use a needle for this method in the operation field after the segmental bronchus has been resected (Figure 2),[2] and some anesthesiologists blow out the air through the targeted bronchus with a thin bronchoscope before the segmental bronchus is resected.[3]

In our department, we had been using the selected segmental inflation technique with needles to avoid bacterial contamination in the operative field and to reduce the anesthesiologist's burden. We had no problems with this method before the present case. However, although no blood reflux was confirmed, the tip of the needle might have moved during inflation at this time with air blown into the vessels, which resulted in ST-segment elevation and diffuse brain edema. After the present case, we started using an "open-cut" method, in which the segmental bronchus is resected and opened, followed by insertion of the outer sheath without the needle, with air then blown into the lumen.

Before this experience, we had never seen such a complication. From the published data, only 1 case with the same complication was reported in 2010 in Japan,[4] which suggests it is extremely rare, but possible, when a needle is used in the selected segmental inflation technique. Thus, we recommend an "open-cut" selected segmental inflation technique without the use of a needle or the use of the selected segmental inflation technique through a thin bronchoscope.

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*Case Report*

# Preferred Surgical Approach for Dumbbell-shaped Tumors in the Posterior Mediastinum

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**We present the case of a 67-year-old male smoker with a posterior mediastinal hemangioma. Radiological findings revealed a dumbbell-shaped tumor with a neuroforaminal extension in the right paravertebral space. Under the preoperative diagnosis of a neurogenic tumor, surgery was performed using a combined anterior and posterior approach. During the thoracotomy, the tumor was found to be a hemangioma. We ligated the involved vessels before performing laminectomy, thus ensuring that complete tumor resection was achieved without massive bleeding in the spinal canal. Dumbbell-shaped hemangiomas are rare, and preoperative confirmation of the diagnosis is challenging. Thoracotomy before laminectomy is optimal for the resection of dumbbell-shaped tumors of the mediastinum, especially with marked vascularity, given that the initial thoracotomy procedures facilitate the subsequent laminectomy procedures.**

**Key words:** dumbbell-shaped tumor, mediastinal hemangioma, thoracotomy

## Introduction

The location of a posterior mediastinal tumor is the key to selecting the surgical approach. When neuroforaminal extension is suspected, a combination of anterior and posterior approaches should be considered for tumor resection. Thoracotomy has been the standard choice for the anterior approach, although thoracoscopic surgery has recently become an option. The order in which the anterior (thoracotomy or thoracoscopic surgery) and posterior (laminectomy) approaches are performed usually depends on the operator's preference[1]; however, based on our experience we recommend thoracotomy before laminectomy.

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## Case Presentation

A 67-year-old male smoker was referred to our hospital for further investigation after an abnormal shadow was found in a chest roentgenogram during an annual screening. His history was unremarkable, and he was asymptomatic neurologically and physically.

The results of the physical examination and blood tests were normal. A chest roentgenogram revealed an egg-sized mass in the right apical lung field. Chest computed tomography (CT) revealed a well-defined oval mass in the right paravertebral space at the level between T2 and T3. The tumor was heterogeneously enhanced with contrast media and had caused scalloping of the vertebral body (**Fig. 1A** and **1B**). Magnetic resonance imaging (MRI) revealed a dumbbell-shaped tumor with a neuroforaminal extension, which had widened the intervertebral foramen (**Fig. 2A** and **2B**). The epidural lesion occupied the right half of the spinal canal, shifting the spinal cord to the left. Based on these radiological findings, the

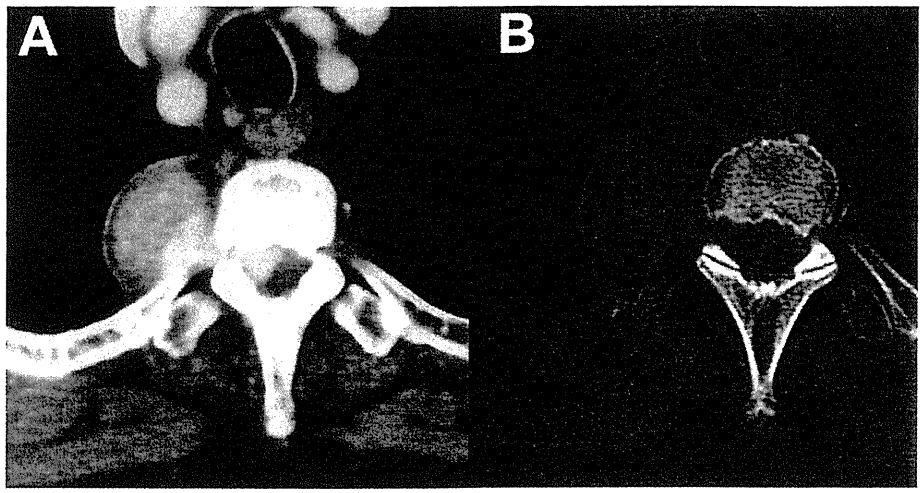


**Fig. 1** Chest computed tomography scans showing a well-delineated mass in the right paravertebral space. The tumor was intensely and heterogeneously enhanced on administration of intravenous contrast medium (**A**). The tumor caused scalloping of the posterior margin of the vertebral body (**B**).

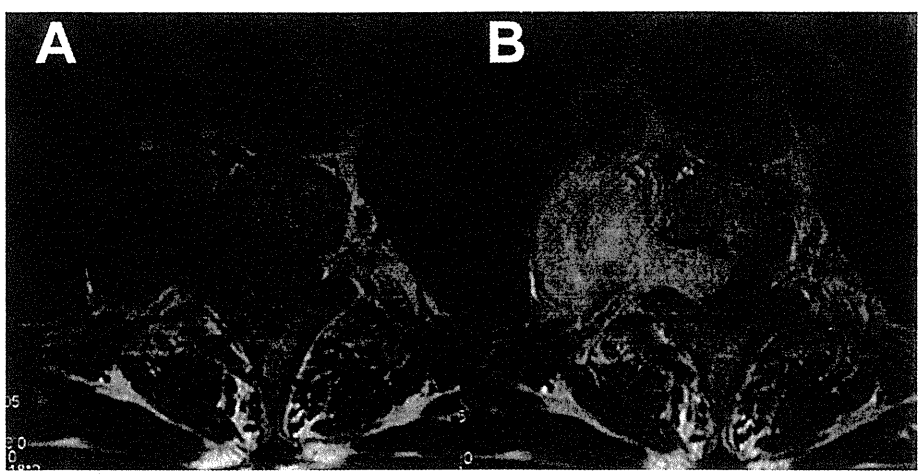


**Fig. 2** Magnetic resonance images showing a tumor with neuroforaminal extension causing widening of the intervertebral foramen. Relative to the spinal cord, the tumor was isointense in T1-weighted images (**A**) and hyperintense in T2-weighted images (**B**).

tumor was presumptively diagnosed as a dumbbell-shaped neurogenic tumor in the right posterior mediastinum.

Single-stage surgery was performed using a combination of thoracic and neurosurgical approaches. First, a right thoracotomy was used to reveal a round, smooth, richly vascular, dark red tumor in the thoracic apex. The involved intercostal arteries and veins were ligated, and the intrathoracic part of the tumor was excised. Part of the sixth costal bone was resected for later spinal stabilization. The frozen section diagnosis was hemangioma. After thoracotomy, neurosurgeons performed laminectomy and facetectomy. The tumor involved the right T2 proximal root and adhered broadly to the dura at the T2 level. The T2 root was sacrificed, and the tumor was completely removed. Spinal stabilization was performed utilizing the costal bone autograft. The patient recovered without any major functional impairment. No sign of recurrence was detected during the 18 months after surgery.

## Discussion

What we learned from this case is that an evaluation of tumor vascularity is essential to decide on a surgical approach for dumbbell-shaped posterior mediastinal tumors. Especially when the tumor shows contrast-enhancement on CT images, it is likely to show marked vascularity. The greatest advantage of performing thoracotomy before laminectomy is to allow us to ligate the involved arteries while the tumor is clearly exposed. Ligation of associated arteries is the most important procedure to achieve complete resection of the tumor without massive bleeding. In addition, since the blood supply to the spinal canal comes from the posterior branches of the intercostal arteries, ligation of the involved arteries facilitates the laminectomy procedure. Massive bleeding in the spinal canal is the most frequent reason for permanent cord injury and incomplete resection of tumors involving the spinal canal.[1, 2] Thoracoscopic surgery is far less suitable than a thoracotomy for managing hemorrhagic tumors. In this case, we first ligated the feeding arteries of the tumor via a thoracotomy, so we were able to complete the tumor resection without major complications. Another advantage of this method is that costal bone can be resected from the same operative site as an autograft, when spinal stabilization is required. Furthermore, there are some limited occasions when the tumor can be resected safely via a thoracotomy without the need for a laminectomy.[1]

Mediastinal hemangiomas are extremely uncommon; they account for no more than 0.5% of all mediastinal tumors,[3] and are very rarely found in the posterior mediastinum.[4] Rather, tumors of the posterior mediastinum tend to be neurogenic,[5] as are most dumbbell-shaped mediastinal tumors.[1] Moreover, it is sometimes difficult to distinguish a hemangioma from a neurogenic tumor, based on the radiological findings. Typical CT findings for hemangioma are reportedly lobulation, heterogeneous enhancement with contrast media, multiple ring-like calcifications and an intact intervertebral foramen when the tumor extends to the spinal canal; however, these findings are not always observed.[4, 6] MRI yields no definitive findings: both neurogenic tumors and hemangiomas are iso- to hypointense in T1 images and homogeneously hyperintense in T2 images.[2, 7] Hemangioma should always be considered in the differential diagnosis of a dumbbell-shaped posterior mediastinal tumor, even though it is a very rare entity.

Endovascular embolization has been recently used to remove a hemangioma, successfully minimizing blood loss during the operation.[8] In a limited occasion, angiography and subsequent endovascular embolization might be appropriate if a tumor is strongly enhanced with contrast media on CT images. However, we should be aware that this management approach is not safe because of the risk of a spinal infarction, especially for a posterior mediastinal tumor locating at the lower level of thoracic vertebrae or extending to the intervertebral foramen.

In conclusion, we suggest that a thoracotomy before a laminectomy is the preferred surgical approach for dumbbell-shaped posterior mediastinal tumors with marked vascularity. Careful radiological evaluation and appropriate preparation to preclude profound bleeding in the spinal canal are necessary to ensure a good surgical course.

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*Case Report*

# Primary Ependymoma in the Posterior Mediastinum

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**A 46-year-old woman was referred to our hospital because of back pain and an abnormality on chest imaging. Chest computed tomography showed a well-delineated tumor in the left paravertebral space. Histological analysis of the resected tumor revealed perivascular pseudorosettes, and immunoreactivity for glial fibrillary acidic protein established the diagnosis of ependymoma. A few cases have been reported in the ovary, broad ligament, sacrococcygeal region, lungs, and mediastinum, but the pathogenesis has not yet been clarified. Female predominance in these tumors and organogenesis of the sites may suggest a key to the pathogenesis.**

**Keywords:** mediastinal tumor, ependymoma, female, embryology

## Introduction

Ependymomas generally arise from ependymal cells of the central nervous system (CNS): the ventricular system, choroid plexus, and central canal of the spinal cord,[1] and less often in the brain parenchyma as a result of migration of ependymal cells from periventricular areas during embryogenesis.[1] They rarely arise in the extra-axial region, outside the CNS. A few cases have been reported in the ovary, broad ligament, sacrococcygeal region, lungs, and mediastinum[2–11]; however, the exact origin of such extra-axial ependymomas has not been clarified.

We treated a patient with an ependymoma in the posterior mediastinum that had no association with the spine. Immunohistochemical analysis of the resected lesion revealed the unique characteristics of this tumor, particularly reactivity for female hormone receptors, which is reportedly common in extra-axial ependymomas.[5]

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## Case Presentation

A 46-year-old female smoker was referred to our hospital because of back pain and an abnormality on chest imaging. She had been well until 6 months earlier, when she developed back pain and was seen by a family doctor without any improvement. Five months later, she had an annual chest screening test, in which an abnormal shadow in the left lung field was noticed on chest X-ray. She also reported weight loss of 3 kg in the previous 3 months.

On examination, vital signs and neurologic examination were unremarkable. Laboratory tests were within the reference range. Chest X-ray revealed a mass in the left middle lung field (**Fig. 1**), and chest computed tomography showed a well-delineated tumor with smooth contours in the left paravertebral space at the T7 to T9 level (**Fig. 2A**). The tumor contained calcification and was heterogeneously and weakly enhanced with intravenous contrast media (**Fig. 2B**). There was no evidence of invasion of the adjacent aortic wall, thoracic vertebrae, or ribs. Magnetic resonance imaging of the chest showed that, compared with the spinal cord, the tumor was iso-intense on T1-weighted images (**Fig. 3A**), and moderately intense with foci of signal heterogeneity on T2-weighted images (**Fig. 3B**). Gadolinium enhancement was moderate and inhomogeneous on T1-weighted images (**Fig. 3C**). Additional CT imaging with myelography indicated no

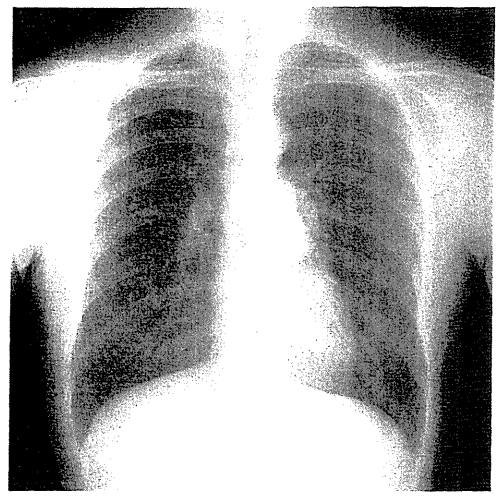

**Fig. 1** Chest X-ray revealing a mass in the left middle lung field.

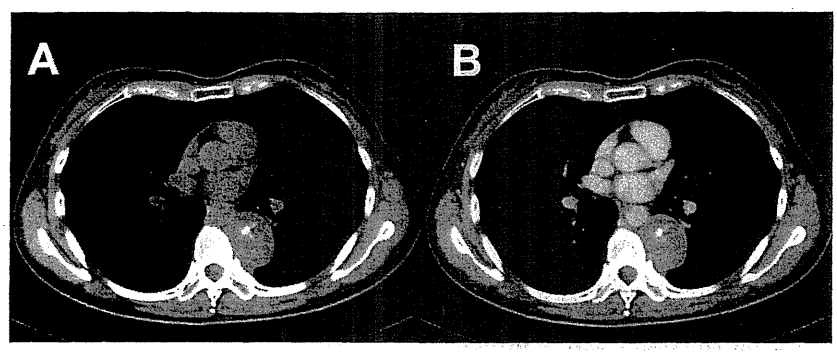


**Fig. 2** **A**: Chest CT showing a well-delineated tumor in the left parasvertebral space. **B**: The tumor contained calcification with heterogeneous and weak enhancement.

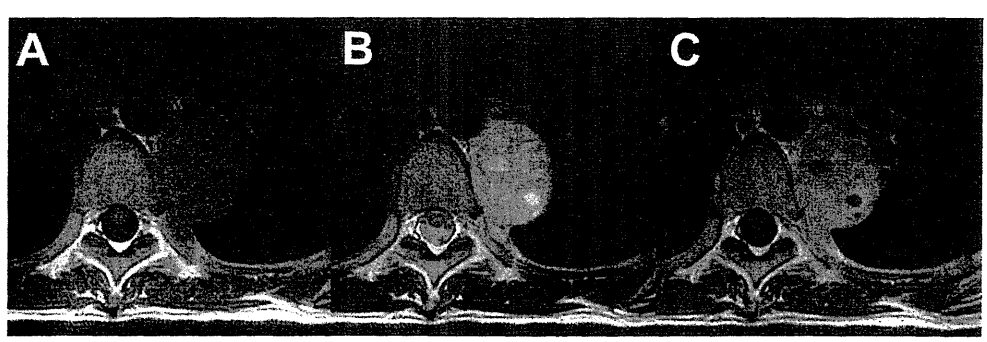


**Fig. 3** **A**) MRI of the chest showing that, compared with the spinal cord, the tumor was iso-intense on T1-weighted images, and **B**) moderately intense with foci of signal heterogeneity on T2-weighted images. **C**) Gadolinium enhancement was moderate and inhomogeneous on T1-weighted images.

involvement of the intervertebral foramens or spine. Via thoracotomy, the tumor was resected en-bloc with the 7th and 8th intercostal muscles and the thoracic sympathetic trunk passing over the tumor.

The resected tumor measured 57 × 47 × 33 mm and weighed 50 g with a lobulated pale yellow cut surface and was encapsulated. Microscopically, the tumor demonstrated solid, trabecular, and cystic architecture and consisted of columnar tumor cells with apically located oval nuclei and elongated fibrillary cytoplasmic processes with moderate nuclear pleomorphism (**Fig. 4A**). Perivascular pseudorosettes and true rosettes were frequently

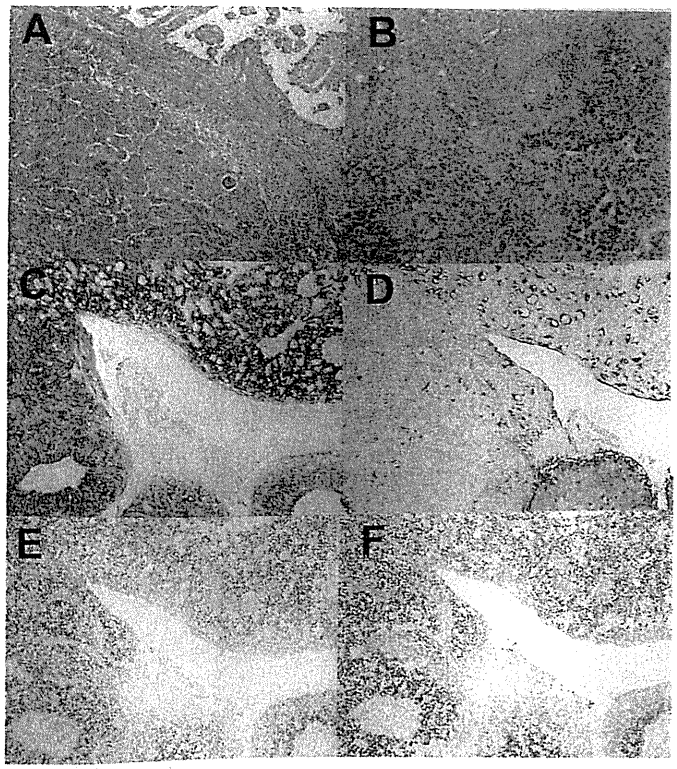


**Fig. 4** Pathological findings of the resected specimens. **A**) Columnar tumor cells with apically located oval nuclei and elongated fibrillary cytoplasmic processes, **B**) perivascular pseudorosettes and true rosettes, **C**, **D**, **E**, and **F**) immunostaining of GFAP, CK7, ER, and PR. Original magnification is × 400 in **B**, and × 100 in **A** and **C** to **F**.

present (**Fig. 4B**). Immunohistochemical analysis showed positive reactivity for glial fibrillary acidic protein (GFAP) (**Fig. 4C**), cytokeratin 7 (CK7) (**Fig. 4D**), and epithelial membrane antigen; and negative reactivity for S-100, CD99, CAM5.2, and CK20. MIB-1 index was up to 15% through the tissue section, and marked immunoreactivity for estrogen and progesterone receptors (ER, PR) was present (**Fig. 4E** and **4F**). Based on these findings, the tumor was diagnosed as primary mediastinal ependymoma, grade II according to the World Health Organization grading.

The postoperative course was uneventful, and the patient was discharged on postoperative day 15 without major complications. She remains well with no sign of recurrence 18 months after surgery.

## Discussion

The posterior mediastinum is a common site for neurogenic tumors, such as neurofibromas and schwannomas, in adults. However, ependymomas at this site are extremely uncommon; to the best of our knowledge, there have been 9 cases reported in the literature including the present case (**Table 1**).[6-11]

Histological and immunohistochemical analysis has indicated differences between CNS and extra-axial ependymomas.[5] Extra-axial ependymomas demonstrate more architectural varieties than their CNS counterparts. The most striking difference is that extra-axial ependymomas preferentially express CK7, CAM5.2, ER, and PR, but do not express CD99, to which CNS ependymomas are strongly immunopositive. Specimens of the present case showed various histological features, with perivascular pseudorosettes and true rosettes frequently observed. Immunohistochemical analysis demonstrated positive reactivity for GFAP, CK7, ER, and PR and negative reactivity for CD99, CAM5.2, and CK20. With the exception of CAM5.2, these features coincide with those mentioned in a previous report.[5]

Immunoreactivity for CK7 and non-reactivity for CK20 generally indicate the site of origin of a given carcinoma, such as the lung, breast, ovary, endometrium, thyroid, or salivary gland.[12] Immunoreactivity for both ER and PR is associated with target organs of female hormones. The present findings suggested a mediastinal metastasis of ovarian ependymoma; however, there was no evidence of such a primary tumor in our patient.

CNS ependymomas are equally distributed between the sexes.[1] Sacrococcygeal ependymomas have the same distribution as CNS ependymomas.[4] However, other

**Table 1 Clinical and pathological features of patients with primary mediastinal ependymoma**

| Case | Age | Sex | Location / Left or Right | Size (cm) | Treatment | Prognosis | ER/PR |
|---|---|---|---|---|---|---|---|
| 1[6] | 51 | F | Paravertebral / Right | 9.0 | Excision + RUL | 4 M, dead | ND |
| 2[7] | 36 | F | Paravertebral / Right | 6.7 | Excision | ND | ND |
| 3[8] | 36 | F | Paravertebral / ND | 7.0 | Excision | 108 M, alive | ND |
| 4[8] | 71 | F | Retrohilar / ND | 5.0 | Excision | 12 M, alive | ND |
| 5[8] | 42 | F | Paravertebral / Left | 6.0 | Excision | 72 M, alive | ND |
| 6[9] | 59 | F | Paravertebral / Left | 4.2 | Excision | ND | ND |
| 7[10] | 39 | F | Paravertebral / Left | 8.0 | Excision | 29 M, alive | ND |
| 8[11] | 50 | F | Paravertebral / Left | 2.8 | Excision | 59 M, alive | +/+ |
| 9 | 46 | F | Paravertebral / Left | 5.7 | Excision | 18 M, alive | +/+ |

ER: estrogen receptor; PR: progesterone receptor; F: female; RUL: right upper lobectomy; M: months; ND: not described

extra-axial ependymomas in the ovary, broad ligament, lung, and mediastinum appear only in women. Sacrococcygeal ependymomas reportedly originate from ependymal rests or coccygeal medullary vestiges.[4] The difference in sex distribution between sacrococcygeal and other extra-axial ependymomas seems to suggest a difference in their pathogenesis.

Primordial germ cells originate from the yolk sac endoderm, and migrate through the cloaca, hindgut, and dorsal mesentery into the gonadal ridge,[13] where the ovary, broad ligament, and sacrococcygeal region develop. Misdirected primordial germ cells have been found in the sacrococcygeal region and mediastinum.[13] One interesting hypothesis is that ependymomas in the ovary, broad ligament, and mediastinum might originate from misdirected primordial germ cells under the influence of female hormones, and this could explain the female predominance of such tumors.

In summary, we have presented a case of primary mediastinal ependymoma. From the clinical, immunohistochemical, and developmental point of view, we suggest that mediastinal ependymomas may originate from misdirected primordial germ cells influenced by female hormones.

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（肺癌．2011;51:777-786）


REPORT

# 日本肺癌学会・日本呼吸器内視鏡学会・日本臨床細胞学会・3学会合同委員会報告：肺門部早期肺癌実態調査アンケート報告

佐藤雅美[1]・斎藤泰紀[1]・渋谷　潔[1]・中山富雄[1]・平野　隆[1]・近藤　丘[1]・馬場雅行[2]・池田徳彦[2]・佐川元保[2]・伊豫田明[2]・宝来　威[2]・中嶋隆太郎[2]・平田哲士[2]・三宅真司[2]・楠　洋子[3]・多田弘人[3]・古川欣也[3]・渡辺洋一[3]

## Early Hilar Type Lung Cancer in Japan: A Survey from January 2006 to December 2007

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***ABSTRACT*** —— ***Background.*** Although sputum cytology is the only way to detect early hilar lung cancer in lung cancer screening, there are also various problems. Therefore, the subcommittees concerning sputum cytology was established in each the Japan Lung Cancer Society and the Japanese Society of Clinical Cytology, and in a joint effort with the Japan Society for Respiratory Endoscopy, the investigation of these problems were reported by the committee of the three societies. We concluded that confirming the usefulness of sputum cytology at present is the inevitable and the most important issue. ***Objective.*** We clarified the actual situation of diagnosis for early hilar lung cancer in Japan by a questionnaire. ***Subject and Methods.*** We sent questionnaires to authorized and associated institutes of the Japan Society for Respiratory Endoscopy, and respondents were questioned concerning the following items. The basic items were a) the number of bronchoscopies performed, b) the number of lung cancer resections, c) the number of diagnoses of new early hilar lung cancer, d) the modes of detection, e) histological type, f) treatment modalities that can be estimated in each institute from 2006 to 2007. Moreover, to the extent possible, we ask them to respond to g) the number of advanced hilar squamous cell carcinomas, h) the number of sputum cytology examinations that were found to be positive or suspected to be positive, i) the number of peripheral lung cancers detected by sputum cytology, j) the number of cancers in otorhinological field or esophageal cancers detected by sputum cytology. ***Results and the Estimated Number of Diagnosis in Japan.*** The questionnaires were sent to 504 authorized and associated institutes of the Japan Society for Respiratory Endoscopy and returned from 308 (61.1%) of them. These institutes, in the cases of primary lung cancer resections, covered 57.1% of the field study result of the Japanese Association of General Thoracic Surgery. A total of 150 diagnosed cases of early hilar lung cancer in a year were reported. By the reported number and the covering ratio, the number of early hilar lung cancer diagnosis was estimated between 154 and 270 cases per year. Also, 4,000 cases of hilar squamous cell carcinoma in a year in Japan were estimated. Concerning the mode of detection, sputum cytology was the most numerous, accounting for 90% of squamous cell carcinomas; however, the rate of early cancer was less than 10% of hilar squamous cell carcinoma, and moreover, there were regional differences in the detection rates. ***Conclusions.*** The national survey of hilar lung cancer suggested that there were 4,000 patients with hilar squamous cell carcinoma at present. However, the ratio of early cancer was less than 10%, and the regional differences in the ratio of early to not early hilar squamous cell carcinoma were also suggested. Based on these, there might have been more opportunities of early diagnosis of hilar lung cancer than were actually diagnosed. Further quality control and much more sputum cytologic examinations for lung cancer screening is recommended.

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***KEY WORDS*** —— Early hilar-type lung cancer, Squamous cell carcinoma, Bronchoscopic examination, Sputum cytology, Lung cancer mass screening

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**要旨 —— 背景.** 喀痰細胞診は肺癌検診において，肺門部早期肺癌の発見のための唯一のスクリーニング法であるが，さまざまな問題点も存在している．このため3学会（日本肺癌学会，日本臨床細胞学会，日本呼吸器内視鏡学会）合同委員会において検討を重ね，アンケートを行った．**目的.** 全国の肺門部（早期）肺癌の確定診断の実態を明らかにする．**対象と方法.** 日本呼吸器内視鏡学会気管支鏡認定施設・関連認定施設にアンケートを送付し，2006年，2007年の気管支鏡検査件数，肺癌切除例数，新規肺門部早期癌診断例数，その発見動機，組織型，治療法を，さらに可能な範囲で肺門部進行扁平上皮癌数，喀痰細胞診陽性・疑陽性による検査件数，喀痰細胞診による末梢型肺癌例数などに関して回答を求めた．**結果.** 504施設にアンケートを送付し308施設より回答を得た．これらの施設は日本胸部外科学会全国集計の57.1%をカバーしていた．年間150例程度の肺門部早期肺癌が報告された．報告数とカバー率から肺門部早期肺癌の全国における初回診断数は年間154～270例程度と推定され，肺門部の扁平上皮癌に関しては全国で年間約4,000例の存在が推定された．しかし，早期癌の比率は肺門部扁平上皮癌全体の10%を下回っていた．さらに，その発見率には地域差が見られた．**考察および結論.** 肺門部肺癌に関しては，現在診断されているよりも，さらに多くの症例で早期診断の機会があったと推測され，肺癌検診のさらなる精度管理や喀痰細胞診の受診勧奨など，検討すべき事項が存在するものと推定された．

**索引用語 ——** 肺門部早期肺癌，扁平上皮癌，気管支鏡，喀痰細胞診，肺癌集団検診

## はじめに

肺癌は本邦においても癌死亡死因の第一位を占めている．喫煙率の低下が報告されている現在においても肺癌死亡は増加を続けており，早期発見による治療が社会的要請となっている．そのため肺癌検診のあるべき姿に向けた議論も活発となっている．[1-4]

肺癌早期発見の手法に関しては，胸部単純X線写真，[1,5-9] 喀痰細胞診，[1,5-19] 胸部CT[1,4,8,9,12,20]などがあり，そのいずれをもってしても完璧なものはなく，併用することにより，より精度の高いスクリーニングが可能となる．[12] 一方で，費用対効果の視点から，その有用性とニーズを見極めることも重要である．[9] 喫煙率の低下が報告されている現状において，喀痰細胞診は本当に必要なのか？ 全世界的に腺癌が増加している現在，喀痰細胞診に要する費用をCTによる検診に振り分けるべきではないか，という議論も見られる．

肺癌検診における喀痰細胞診に関しては，有用性を報告する施設が見られるものの，一方で発見例の減少を示唆する施設や，喀痰細胞診の併用を中止する市町村が出現するなど，さまざまな混乱や問題点が存在する．[10] これらに対応すべく，日本肺癌学会では，集団検診委員会内に喀痰細胞診による肺癌検診小委員会を，また，日本臨床細胞学会では総務委員会内に肺癌検診ワーキンググループを設置し，2つの委員会の合同委員会で検討を重ねてきた．検討を重ねる中で，喀痰細胞診による早期発見を必要とする肺門部扁平上皮癌の実態を把握することが今後の対応を決める上で最も緊急かつ重要であるとの共通認識に至った．一方，著者らが知りうる範囲においては本邦における肺門部肺癌の実態は，系統だった調査や大規模な統計などで研究・公表されたものはなかった．そこで，前述の2学会に加え，日本呼吸器内視鏡学会学術企画委員会を中心とした肺癌検診ワーキンググループとともに，肺門部早期肺癌実態調査アンケートを行い，多くの施設の多大な協力の下に回答を集計することができたので，ここに報告する．

## 対象と方法

日本肺癌学会集団検診委員会喀痰細胞診による肺癌検診小委員会，日本臨床細胞学会総務委員会肺癌検診ワーキンググループ，および日本呼吸器内視鏡学会学術企画委員会肺癌検診ワーキンググループの合同会議でアンケート項目の検討を行い，2006，2007年（平成18，19年）における各施設の，a）気管支鏡検査件数，b）肺癌切除例数，c）新規肺門部早期癌診断例数，d）その発見動機，e）組織型，f）治療法，を必須回答項目とした．さらに可能な範囲で，a）肺門部進行扁平上皮癌数，b）喀痰細胞診陽性・疑陽性による検査件数，c）喀痰細胞診による末梢型肺癌発見例数，d）喀痰細胞診による耳鼻科領域癌発見例数・食道癌発見例数，に関しても回答を求めた（Table 1）．

アンケートの配布先は，日本呼吸器内視鏡学会気管支鏡認定施設および関連認定施設（計504施設）の気管支鏡検査責任者宛とした．アンケートは2009年（平成21年）1月10日に発送し，アンケートの回収期限を2009年（平成21年）2月28日としたが，最終的にはアンケート督促状配布を2009年3月30日に行い，アンケート最終締め切りを2009年4月30日とした．

また，アンケート回収施設における原発性肺癌切除例数と日本胸部外科学会で施行している毎年の全国集

**Table 1.** Items of the Japanese National Survey of Early Hilar Lung Cancer

Study period: 2006-2007
1) Basic items
  a) Number of bronchoscopies performed
  b) Number of lung cancer resections
  c) Number of diagnoses of new early hilar lung cancer
  d) Modes of detection
  e) Histological type
  f) Treatment modalities

2) Others
  a) Number of advanced hilar squamous cell carcinomas
  b) Number of sputum cytology examinations found to be positive or suspected to be positive
  c) Number of peripheral lung cancers detected by sputum cytology
  d) Number of cancers in otorhinological field or esophageal cancers detected by sputum cytology

**Table 2.** Annual Numbers

| Current survey results | 2006 | 2007 |
|---|---|---|
| Bronchoscopies | 64,250 | 65,584 |
| Lung cancer resections (A) | 14,670 | 15,356 |
| New early hilar lung cancers | 155 | 152 |
| The number of primary lung cancer resections in Japan surveyed by the Japanese Association for Thoracic Surgery (B) | 26,531 | 26,092 |
| The reported ratio (A/B) of the current questionnaire | 55.3% | 58.9% |
| Throughout 2006 and 2007 | 57.1% | |

計[21,22]から，これらの施設の肺癌切除例数の比率を算出し，日本全国で発生する肺門部進行扁平上皮癌数と肺門部早期肺癌数を推定した．

## 結　果

**1）アンケートの回収状況**

2009年3月31日までに165施設（32.7%）より回答があった．2009年4月30日までには72施設（14.3%）から回答が追加で送られ，2009年5月18日までにはさらに71施設（14.1%）より回答があった．総計では，308施設（61.1%）よりの回答を得た．

**2）回答施設における気管支鏡検査数，肺癌切除例数，新規肺門部肺癌診断数**（Table 2）

回答施設における気管支鏡検査数は2006年64,250件，2007年65,584件であった．同様に原発性肺癌切除例数は2006年14,670例，2007年15,356例であった．日本胸部外科学会で施行している毎年の全国集計に占めるこれらの施設の肺癌切除例数の比率は2006年55.3%（14,670/26,531），2007年58.9%（15,356/26,092）で，2年間通年では57.1%であった．回答施設における新規肺門部早期肺癌の診断例数は2006年155例，2007年152例であった．

肺門部早期肺癌の診断例がなかった施設数は2006年238施設（77.3%），2007年238施設（77.6%）であった．

**3）肺門部早期肺癌例の発見動機**（Table 3）

肺門部早期肺癌例の発見動機別に見ると2006年は喀痰細胞診によるもの93例，うち検診時発見例59例，血痰26例，他疾患観察時の気管支鏡検査によるもの31例，その他22例，不明16例であった．2007年は喀痰細胞診によるもの69例，うち検診時発見例36例，血痰32例，他疾患観察時の気管支鏡検査によるもの23例，その他24例，不明10例であった．2年間を通して喀痰細胞診発見例が最多を占めていた．

**4）肺門部早期肺癌例の組織型**（Table 4）

扁平上皮癌が2006年140例，2007年135例と大部分を占めた．ごく少数ながら非扁平上皮癌も見られた．

**Table 3.** Modes of Detection

| Modes of detection | 2006 | 2007 |
|---|---|---|
| Sputum cytology | 93 | 69 |
| Sputum cytology in population-based mass screening | 59 | 36 |
| Bloody sputum | 26 | 32 |
| Bronchoscopies performed for other pulmonary disorders | 31 | 23 |
| Others | 22 | 24 |
| Unknown | 16 | 10 |

**Table 4.** Histological Type

| Histological type of early hilar lung cancer | 2006 | 2007 |
|---|---|---|
| Squamous cell carcinoma | 140 | 135 |
| Adenocarcinoma | 5 | 6 |
| Large cell carcinoma | 0 | 2 |
| Small cell carcinoma | 5 | 3 |
| Others | 1 | 3 |
| Unknown | 4 | 3 |

**5) 肺門部早期肺癌例の初回治療法**（Table 5）

肺門部早期肺癌例の主たる初回治療法は，2006年では手術[6]が49例，PDTレーザー[23,24]が66例，外照射が17例であった．腔内照射と化学療法が各3例で，無治療例が8例見られた．2007年では手術が59例，PDTレーザーが45例，外照射が26例であった．腔内照射は4例で，化学療法が13例，無治療例が5例見られた．手術，PDTレーザーが大半を占め，次いで外照射が続いた．

**6) 肺門部進行肺癌例数**（Table 6）

以下，Table 11まで可能な範囲で回答を寄せた施設の集計である．これらの施設における早期肺癌の定義を満たさない肺門部扁平上皮癌の診断数は2006年には1,222例，2007年には1,270例であった．

**7) 喀痰細胞診陽性または疑陽性で気管支鏡検査の対象となった症例数**（Table 7）

喀痰細胞診陽性で気管支鏡検査の対象となった症例数は2006年には689例，2007年672例であった．一方，疑陽性の症例数は2006年439例，2007年411例で，その合計は2006年1,128例，2007年1,083例であった．

**Table 5.** Initial Treatment

| Initial treatment for early hilar lung cancer | 2006 | 2007 |
|---|---|---|
| Surgery | 49 | 59 |
| PDT laser | 66 | 45 |
| Laser apart from PDT | 6 | 2 |
| Brachytherapy | 3 | 4 |
| External irradiation | 17 | 26 |
| Chemotherapy | 3 | 13 |
| Untreated | 8 | 5 |
| Others | 1 | 3 |
| Unknown | 0 | 1 |

**Table 6.** Cases of Progressive Hilar Squamous Cell Carcinoma

| | 2006 | 2007 |
|---|---|---|
| Advanced hilar squamous cell carcinoma | 1,222 | 1,270 |

Appendix: All cases of hilar squamous cell carcinoma not defined as early hilar lung cancer were considered to be advanced hilar squamous cell carcinoma.

**Table 7.** Number of Cases Which Required Bronchoscopic Examination Due to Positive or Suspected to Be Positive Findings on Sputum Cytology*

| | 2006 | 2007 |
|---|---|---|
| Positive findings on sputum cytology | 689 | 672 |
| Suspected to be positive findings on sputum cytology | 439 | 411 |
| Total | 1,128 | 1,083 |

*Including cases in which pathological changes were not seen on bronchoscopy.

**8) 喀痰細胞診が発見動機となった末梢型肺癌および耳鼻科領域癌，食道癌の症例数**（Table 8，9）

喀痰細胞診が発見動機[15]となった末梢型肺癌は2006年203例，2007年225例であった．また喀痰細胞診が発見動機[13]となった耳鼻科領域癌は2006年20例，2007

**Table 8.** Number of Cases with Peripheral Lung Cancer Detected by Sputum Cytology

| | 2006 | 2007 |
|---|---|---|
| Peripheral type lung cancer detected by sputum cytology | 203 | 225 |

**Table 9.** Number of Otorhinological or Esophageal Cancer Detected by Sputum Cytology

| | 2006 | 2007 |
|---|---|---|
| Otorhinological cancers detected by sputum cytology | 20 | 11 |
| Esophageal cancers detected by sputum cytology | 7 | 5 |

**Table 10.** The Ratio of Early to Advanced Hilar Squamous Cell Carcinoma

| | 2006 | 2007 |
|---|---|---|
| Responding institutions | 179 (58.1%) | 181 (59.0%) |
| Total number of bronchoscopies performed | 37,027 | 38,242 |
| Early hilar squamous cell carcinoma | 121 (9.1%) | 99 (7.2%) |
| Advanced hilar squamous cell carcinoma | 1,222 (90.9%) | 1,270 (92.8%) |

年 11 例であり，同様に喀痰細胞診が発見動機となった食道癌は 2006 年 7 例，2007 年 5 例であった．

**9）報告施設における肺門部早期扁平上皮癌，非早期扁平上皮癌の比率**（Table 10）

オプションとした（あるいは，回答が可能な施設での）アンケート項目である肺門部非早期癌の診断数の報告は 2006 年 179 施設（58.1%），2007 年 181 施設（59.0%）から得られた．これらの施設における早期/非早期の比率は 2006 年肺門部早期扁平上皮癌 121 例（9.1%），肺門部非早期扁平上皮癌 1,222 例（90.9%），2007 年肺門部早期扁平上皮癌 99 例（7.2%），肺門部非早期扁平上皮癌 1,270 例（92.8%）であった．

**10）地域別に見た肺門部肺癌における早期癌の比率**（Table 11）

地域別に見た肺門部扁平上皮癌における早期癌の比率は北海道 37/221（16.7%），東北 27/186（14.5%），関東 94/934（10.1%），東海 16/291（5.5%），甲信越 18/137（13.1%），北陸 21/93（22.6%），近畿 17/419（4.1%），中国 15/109（13.8%），四国 13/79（16.5%），九州・沖縄 17/297（5.7%）であった．2×10 のカイ 2 乗検定では，地域間格差が見られた（$p<0.0001$）．

**Table 11.** Ratio of Early Cancer to Total Cases of Hilar Squamous Carcinoma in Each Japanese Region

| Region | Early cancer / Total hilar type squamous cell carcinoma | % |
|---|---|---|
| Hokkaido | 37/221 | 16.7 |
| Tohoku | 27/186 | 14.5 |
| Kanto | 94/934 | 10.1 |
| Tokai | 16/291 | 5.5 |
| Koshinetsu | 18/137 | 13.1 |
| Hokuriku | 21/93 | 22.6 |
| Kinki | 17/419 | 4.1 |
| Chugoku | 15/109 | 13.8 |
| Shikoku | 13/79 | 16.5 |
| Kyushu・Okinawa | 17/297 | 5.7 |

$p<0.0001$.

**11）日本全国における肺門部進行扁平上皮癌推定診断数と肺門部早期肺癌推定診断数**（Table 12）

肺門部進行扁平上皮癌診断数についてアンケートに回答した施設における原発性肺癌切除例数と，日本胸部外科学会で施行している毎年の全国集計[21,22]から，これらの施設の肺癌切除例数の比率を算出し，日本全国で発生する肺門部進行扁平上皮癌数を推定した．肺門部進行扁平上皮癌診断数についてアンケートに回答した施設は平均 180 施設，これらの施設における非早期肺門部扁平上皮癌の診断数は平均 1,246 例であった．これらの施設の肺癌切除例における日本全体の肺癌切除例に占める割合は平均 32% であった．これらより，日本全国では年間あたり 3,894 例の非早期肺門部扁平上皮癌が診断されていると推定された．

同様に早期肺門部扁平上皮癌の診断数について推定すると，肺門部早期扁平上皮癌について回答を寄せた施設は平均で 154 施設で，これらの施設の肺癌切除例数は日本全体の 57.1% をカバーしていた．このことより年間平均で 270 例の肺門部早期扁平上皮癌の診断例の存在が推定された．しかしながら，アンケートに回答した施設が早期肺門部扁平上皮癌の診断の熱意のある施設のみである可能性も否定し得ないため，3 学会合同の委員会では，早期肺門部扁平上皮癌の推定診断数については 154～270 という幅を持たせた表記として報告することとした．

## 考　察

喀痰細胞診は肺癌検診において，肺門部早期肺癌の発見のための唯一のスクリーニング法であるが，さまざまな問題点も包含している．このため日本肺癌学会および

**Table 12.** Estimated Number of Patients with Hilar Type Squamous Carcinoma in Japan

| | 2006 | 2007 | Average |
|---|---|---|---|
| Responding institutions with data about advanced hilar squamous cell carcinoma | 179 | 181 | 180 |
| Advanced hilar squamous cell carcinoma (A) | 1,222 | 1,270 | 1,246 |
| Lung cancer resections performed at responding institutions (B) | 8,043 | 8,686 | 8,365 |
| National lung cancer resections based on survey by the Japanese Association for Thoracic Surgery (C) | 26,531 | 26,092 | 26,312 |
| The covering ratio of the responding institution in Japan (D = B/C) | | | 32% |
| Estimated number of patients with advanced hilar squamous cell carcinoma in Japan (E = A/D) | | | 3,894 |
| The responding institutions with data about early hilar squamous cell carcinoma (F) | 308 | 308 | 308 |
| Early hilar squamous cell carcinoma (G) | 155 | 152 | 154 |
| Lung cancer resections at responding institutions (H) | 14,670 | 15,356 | 15,013 |
| National lung cancer resections based on survey by the Japanese Association for Thoracic Surgery (C) | 26,531 | 26,092 | 26,312 |
| The reported ratio of the responding institutions in Japan (I = H/C) | | | 57.1% |
| Maximum estimated number of early hilar lung cancer in Japan (J = G/I) | | | 270 |
| Estimated number of early hilar lung cancer cases in Japan | | | 154-270 |

日本臨床細胞学会内に喀痰細胞診に関する小委員会が設置され，合同の委員会において検討が重ねられた．さまざまな視点からの問題点の発掘や提案の中で，喀痰細胞診による早期発見を必要とする肺門部扁平上皮癌の実態を把握することが今後の対応を決める上で最も緊急かつ重要であるとの結論に至り，本アンケートを行った．

背景には，肺癌死亡の増加を止めきれていない日本の現況やCT検診への期待と不安，喫煙率の変化に伴う罹患構造の変化へどう対応するか，喀痰細胞診による肺癌発見例の減少を報告する施設がある一方で不変であるとする施設が見られるなど，さまざまな混乱や不安などがあったと思われる．一方，著者らが知りうる範囲においては本邦における肺門部肺癌の実態は，系統だった調査や大規模な統計などで研究・公表されたものはなかった．すなわち，我々は推論に基づく，あるいは根拠の希薄な個々の限られた経験に基づく主張をそれぞれの立場で繰り返していた．合同委員会では，今回，このような反省と視点に基づき，全国実態調査を企画した．

一方，アンケートでは，回答施設での負担を考慮し，必須回答を求めたものと，可能であれば協力をお願いしたものが存在した．このため，本報告では必須回答からの解析と，部分施設での回答からの解析の2通りとなっている．

今回の全国実態調査で判明した主な点を簡単にまとめると，

1）年間150例程度の肺門部早期肺癌の診断例が報告された．

2）早期癌の発見動機としては喀痰細胞診が最も多く，ついで血痰，他疾患時の気管支鏡検査時に偶然発見されたものが続いた．

3）組織型としては扁平上皮癌が90%を占めた．

4）治療法としてはレーザーと手術が大半を占めていた．

5）喀痰細胞診により発見された肺門部早期癌より多数の末梢型肺癌や，耳鼻科領域癌，食道癌なども，喀痰細胞診が契機となり発見されていた．

6）肺門部扁平上皮癌において早期の比率は10%を下回っていた．

7）肺門部扁平上皮癌における早期癌の比率には，地域別に検討すると有意差が見られた．

また，肺癌切除例数を利用して日本全国の罹患数を推定すると，

1）肺門部早期肺癌の全国における初回診断例数は年間154～270例程度と推定された．

2）全国では年間約4,000例（3,894＋（154～270））の肺門部扁平上皮癌の存在が推定された．

これらの結果から，喀痰細胞診が肺門部早期肺癌の発見動機として主要な位置を占めていることが伺えた．さらに，喀痰細胞診により発見された早期肺門部肺癌よりも多数の末梢型肺癌や，耳鼻科領域癌，食道癌なども発見されていた．喫煙率の低下が報告されている中，今なお，日本全体では年間4,000例近い肺門部扁平上皮癌が発生していることも重要な事実である．今後の集団検診における喀痰細胞診の位置付けをめぐる議論の中において，客観的数値としての意義は少なくない．今回肺門部扁平上皮癌例数の全国推計値が初めて算出されたことになるが，これが果たして，今後どのように推移していくのか，あるいは地域により罹患数が異なるのか否か，などを検討していく必要がある．

一方，肺門部扁平上皮癌において早期の比率は10%を下回っていたこと，早期癌の比率に地域間格差が存在したことは大きな問題点と考えられた．がん医療の均てん化が叫ばれる中，地域差が見られることは，改めて，その必要性・重要性を喚起しなければならない．むろん，精度管理の重要性に関しては論を待たない．[25] しかし，精度管理の重要性に関しては，すでにこの20年間，繰り返し，述べられてきた．[25-29] その上でのこの実態であることを考慮すると，喀痰細胞診に関しては，現状の精度管理は機能不全に陥っていると言わざるを得ない．従来の考え方，手法を乗り越えたものを目指す必要がある．この点に関しては，さらに議論が必要と考える．

ちなみに喀痰細胞診の感度に関する複数の検討では，喀痰細胞診の感度は少なくとも70%程度[11,14]であり，改善の余地が相当程度にあると推察されうる．

## 推定値の妥当性についての議論

合同委員会においては，推定値の妥当性に関する議論も行われた．まず，アンケートであるため，回答は自主的に行われた．このためのバイアスの存在も危惧された．全数調査でないことも明らかであった．

今回のアンケートでは，気管支鏡の認定施設および関連認定施設にアンケートが配布され，その61.1%にあたる308施設からの回答を得た．これらの施設における気管支鏡検査件数は年平均64,917件であった．2007年に日本呼吸器内視鏡学会安全対策委員会が施行した2006年の気管支鏡の実態調査では，アンケートに回答した375施設で74,770件の気管支鏡検査が報告[30]されており，今回の我々の数値と近似した報告となっている．また原発性肺癌の回答施設の切除例数は年平均15,013であり，日本胸部外科学会の全国集計における原発性肺癌切除例数に占める割合は平均で57.1%であった．本アンケートは全数調査ではないものの，気管支鏡検査実施施設および原発性肺癌切除例数において，少なくとも日本の約半数以上をカバーしたものである．

本報告では，日本胸部外科学会の全国集計における原発性肺癌切除例数に占める割合を，種々の推定を行う場合のカバー率として採用している．日本全体における肺癌切除例数における各施設の比率，気管支鏡検査における各施設の比率，扁平上皮癌の診断数における各施設の比率，さらには早期扁平上皮癌診断例数における各施設の比率が同等であると仮定している．前述のように切除例数における比率と気管支鏡施行例数の比率はほぼ一致しており，極端に大きな問題はないものと考えられた．米国におけるような全国的がん統計を有していない日本では，現状把握が著しく困難である．

また委員会では，集計された肺門部非早期（進行）扁平上皮癌には末梢発生も入っており，そのために真実よりも多い数値が計上されているのではないか，という疑問が出された．末梢発生のものが紛れ込む場合には，以下の3つの場合が主と考えられる．

（ア）4ないし5次気管支発生のいわゆる中間型であれば，増大すれば肺門型として計上されることは十分にあり得る．しかしながら，そのような中間型の早期癌は，定義的には「非肺門型」であっても，喀痰細胞診の対象なので，この調査の対象としては「肺門型」として扱っても問題はないと判断した．

（イ）一方，全くの末梢発生で肺門リンパ節に転移し，さらに気管支に浸潤してきた，というようなものが計上されることも否定できないが，多くは末梢に大きな陰影があるため，末梢型で肺門リンパ節転移ありと正しくカウントされる可能性が高いと思われる．

（ウ）末梢発生だが距離的には太い気管支に近接している，というようなものの場合には，増大することによって肺門と一塊になり肺門型として計上されることはあり得る．ただし，腺癌・大細胞癌などは最初から除外されているので，末梢型扁平上皮癌でそのような増大形式をとった場合ということになる．

上記（ア）（イ）（ウ），特に問題になるのは（ウ）のような場合であるが，その頻度は不明だが，著しく多いとは思えない．頻度が不明なことと他に適当な推定の材料がないことから，このような問題があることは踏まえつつ，ここでは「集計された肺門部非早期（進行）扁平上皮癌を肺門部あるいは中間部発生とする」と仮定することとした．

さらに，日本胸部外科学会の全国集計に関しての指摘も見られた．日本胸部外科学会非認定施設で切除されている分は，この推計では無視した．それに伴い，今回の推定値は若干過少推定になっている可能性がある．また，肺門部進行扁平上皮癌数を答えた180施設とそれ以外の施設における「肺門部進行扁平上皮癌数と，切除肺癌数

の割合」はおおむね同様の傾向を示すと仮定している．当該180施設における肺門部進行扁平上皮癌数の割合がそれ以外の施設よりも高い場合には，国内で発生する肺門部進行扁平上皮癌数は過大に推定され，逆にそれ以外の施設よりも低い場合には，国内で発生する肺門部進行扁平上皮癌数は過少に推定されている可能性がある．

肺門部早期扁平上皮癌数に関しても同様の可能性が考えられる．すなわち，肺門部早期扁平上皮癌の診断例はある程度専門の病院に集まる傾向があるため，切除肺癌数と同様の傾向を示さない可能性がある．したがって，最小推定値として「アンケートの集計値そのもの」，最大推定値として肺癌切除例数から求めた推定値を用いることとした．

このように推定手法に由来する推定値の巾が存在しうるものの，今回，現時点における全国の肺門部扁平上皮癌の診断実態が3学会の学会員および気管支鏡診断施設における協力により，本邦において初めて明らかになったことの意義は大きいと考えられる．

今後疾病構造の変化により疾患の罹患頻度がどのように変化していくのか，肺癌検診と精度管理の必要性が説かれて20年以上の長きにわたるにもかかわらず，早期癌の段階で発見される頻度が10% 以下であること，地域間格差が見られる可能性があることなどから，今後進めるべき精度管理のあり方など，我々が考えるべき課題は大きい．

米国よりCT検診が喫煙者に対して有効であるという報告[4]がなされているその一方で，東京から肺癌をなくす会の検討では，発見された扁平上皮癌の2/3で喀痰細胞診が陽性であり，なかんずく1/3はCTは陰性で喀痰細胞診のみが陽性であった．[12] このことはCTによるスクリーニングの限界をも示している．肺癌早期発見の手法に関しては，いずれの方法をもってしても完璧なものはなく，併用することにより，より精度を高く維持できると考えられる．非喫煙者肺癌に比べて予後が不良と言われる喫煙者肺癌に，今後我々はどのように向き合うか，も問われている．

以上，今回のアンケートにより明らかとなった肺門部扁平上皮癌の本邦における診断実態を報告した．本アンケートの結果が日本の肺癌診療の向上に寄与することを期待したい．

本論文内容に関連する著者の利益相反：平田哲士［企業の職員・法人の代表］NPO法人セルサイト，渡辺洋一［企業の職員・法人の代表］NPO法人新しい医療技術を普及させる会．馬場委員については，やむを得ざる事情を勘案し，編集委員会委員長および利益相反管理委員会委員長の判断により，特例としてCOI報告を免除した．

本報告は3学会合同委員会報告であり，それぞれの学会雑誌に各学会の小委員長名で掲載される．

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