Two Cases of Small Cell Lung Cancer Presenting an Unusual Pattern of Progression Mimicking Pleural Mesothelioma

Yoshinobu Maeda,[1] Yoshihiko Segawa,[1,2]* Nagio Takigawa,[1,2] Ichiro Takata,[1] Nobukazu Fujimoto,[1] Katsuyuki Hotta,[1] Koichi Mandai,[2,3] and Kenji Eguchi[1,2]

Departments of [1]Internal Medicine, [2]Clinical Research, and [3]Pathology, National Shikoku Cancer Center Hospital, Matsuyama, Japan

We describe 2 cases in which small cell lung cancer presented an unusual pattern of progression that mimicked malignant pleural mesothelioma on diagnostic imaging. The patients were a 74-year-old man and a 69-year-old woman, both of whose chest roentgenograms and CT scans showed irregular right pleural thickening with effusion. Small cell lung cancer had been diagnosed by routine examination in the former patient, but the latter had been given a clinical diagnosis of pleural mesothelioma until postmortem examination, which showed small cell lung cancer. The right lung of each patient was found to be fused to the thorax by a thick layer of tumor cell involvement on postmortem examination.

Int J Clin Oncol 1998;3:121–124

Key words: small cell lung cancer, pleural involvement, malignant pleural mesothelioma, postmortem examination

INTRODUCTION

Small cell lung cancer occurs within the center of the lung more often than in the periphery. "Pseudomesotheliomatous" carcinoma, as termed by Harwood et al., is a distinct variant of peripheral lung cancer that is characterized by extensive pleural growth.[1] Therefore, lung cancer resembling malignant pleural mesothelioma is most frequently observed in patients with adenocarcinoma, and only infrequently in those with small cell carcinoma. We present 2 autopsy-confirmed cases in which small cell lung cancer presented an unusual pattern of progression that mimicked malignant pleural mesothelioma on diagnostic imaging.

CASE REPORT

Case 1

A 74-year-old man was admitted to our hospital on July 7, 1992 for progressive dyspnea and cough. He had been a shipper for about 25 years. He was a heavy smoker (smoking index, 2300) and had a history of pneumonia at the age of 5 years. A chest roentgenogram obtained in April 1989 showed postinflammatory changes in both upper lung fields.

Received Feb. 28, 1997; revised Sep. 2, 1997; accepted for publication in revised form Sep. 24, 1997. *Correspondence and requests for reprints to: Departments of Internal Medicine and Clinical Research, National Shikoku Cancer Center Hospital, 13 Horinouchi, Matsuyama 790-0007, Japan.

Physical examination showed no abnormal findings except for diminished breath sounds in the right lower chest. The results of the complete blood count and blood chemistry tests were normal. Tumor marker analysis disclosed an increased carcinoembryonic antigen level (18.5 ng/mL). Pulmonary function test results showed a restrictive pattern of disturbance (percentage vital capacity, 64.4%; forced expiratory volume in 1 second, 72.6%), and arterial blood gas analysis showed hypoxemia (partial pressure of arterial oxygen [PaO_2], 53.7 mm Hg; partial pressure of arterial carbon dioxide, [$PaCO_2$] 35.3 mm Hg).

A chest roentgenogram obtained on admission showed irregular right pleural thickening and effusion with right hilar lymphadenopathy (Fig. 1A). CT scans of the chest showed an extensive progression of tumor to the right pleura (Fig. 2A). Right pleural effusion and mediastinal lymphadenopathy were also found. Bronchoscopic examination showed the right basal endobronchus stenotic due to submucosal involvement of tumor. Histologic examination of the biopsied tumor specimen showed small cell carcinoma. There were no lesions suggesting extrathoracic metastases, therefore the patient's disease was T4, N2, M0, stage IIIB.

The patient underwent combination chemotherapy consisting of carboplatin and etoposide every 4 weeks, and achieved a partial response. He was discharged from our hospital on November 2, 1992. However, he was readmitted 2 months later due to a rapid recurrence of the disease and underwent salvage chemotherapy. This chemotherapy was not effective, and he died on February 3, 1993.

1341-9625/98/0302-0121/US$3.00

On postmortem examination, the right lung was tightly fused to the thorax and the underlying diaphragm was covered by a thick layer of gray-white tissue (Fig. 3A). The gross intrathoracic appearance was of malignant pleural mesothelioma. The primary tumor was in the right lower lobe, separate from the thickened pleura. On histologic examination, the layer between the lung and thorax was found to be composed of small cell carcinoma. The contralateral lung did not adhere to the thorax, although small metastatic nodules were present within it.

Case 2

A 69-year-old woman was admitted to our hospital on December 12, 1994 for dyspnea. She was a farmer and she smoked tobacco (smoking index, 350). She had been healthy, with no respiratory symptoms, until 2 weeks prior to admission, when she noted progressive dyspnea.

On physical examination, she was emaciated and had a low-grade fever (37.2°C). Breath sounds were decreased in the right chest. The complete blood count and blood chemistry test results were normal except for an increased erythrocyte sedimentation rate (70 mm/h). Tumor marker analysis showed an increased neuron-specific enolase level (11.5 ng/mL). Arterial blood gas analysis showed hypoxemia (PaO_2, 57.1 mm Hg; $PaCO_2$, 32.8 mm Hg).

A chest roentgenogram obtained on admission showed massive right pleural effusion, and pleural thickening was seen after tube thoracocentesis (Fig. 1B). CT scans of the chest showed dissemination of tumor to the right pleura (Fig. 2B). Hilar and mediastinal lymphadenopathy was also present.

A cytologic examination of the right pleural effusion showed malignant tumor cells. However, the type of

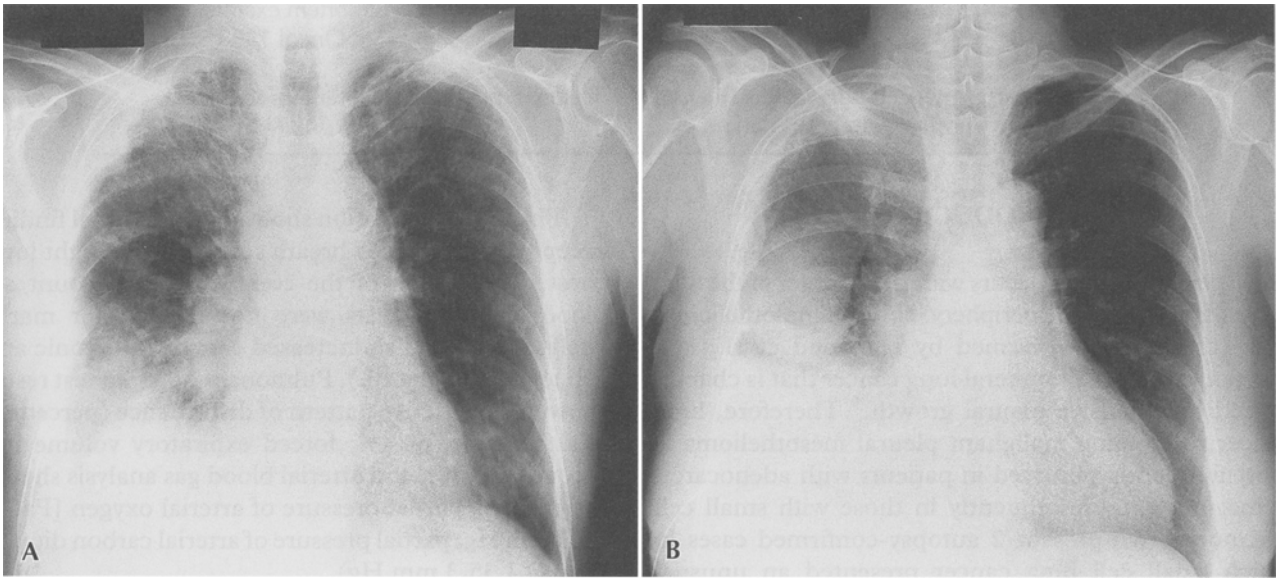

Fig. 1. Chest roentgenograms showing right pleural thickening and effusion: (**A**) on admission in a 74-year-old man (case 1); (**B**) after tube thoracocentesis in a 69-year-old woman (case 2).

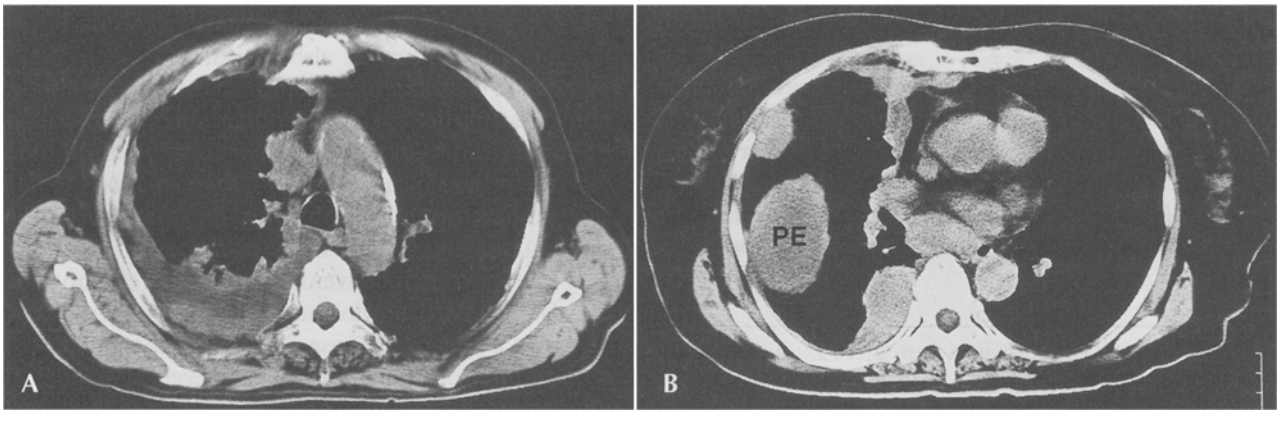

Fig. 2. CT scans of the chest showing dissemination of tumor to the right pleura: (**A**) case 1; (**B**) case 2. Encapsulated interlobar pleural effusion (PE) was also present in case 2.

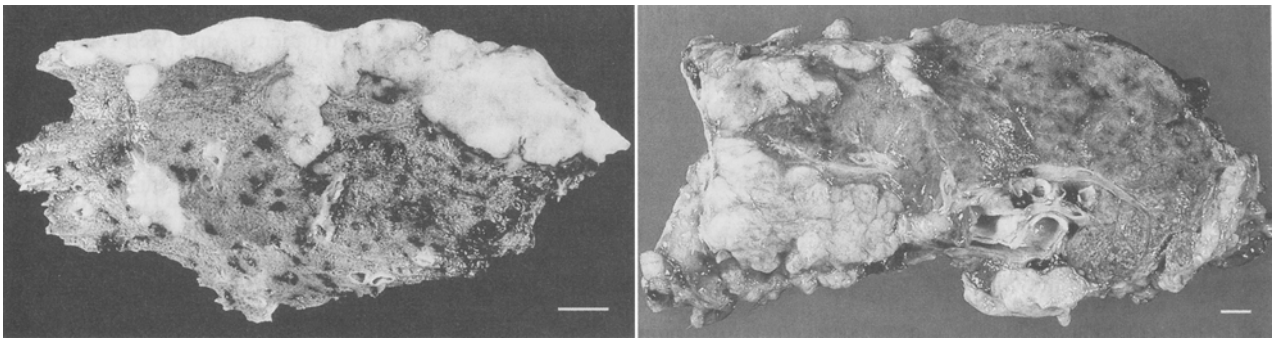

Fig. 3. Cut surfaces of right lung on postmortem examination: (**A**) case 1; (**B**) case 2. Bars equal 1 cm.

tumor could not be determined due to severe degradation of the cells. In addition, a biopsied sample of the pleura showed mesothelial hyperplasia. The possibility of malignant pleural mesothelioma could not be excluded based on examination of this material. Bronchoscopic examination was not performed due to the patient's poor condition.

There were no extrathoracic lesions detected on the examinations performed. Therefore, she was given the clinical diagnosis of malignant pleural mesothelioma. She did not undergo any anticancer therapy other than tube thoracocentesis. Her condition deteriorated rapidly and she died on March 3, 1995.

On postmortem examination, the right lung was fused to the thorax by a thick layer of fragile white tissue (Fig. 3B). This tissue extended to the diaphragm, mediastinum, and pericardium. On histologic examination, the tissue was found to be composed of small cell carcinoma. Massive invasion of tumor cells to vascular and lymphatic spaces was also present. The primary tumor was not found. The contralateral lung did not adhere to the thorax.

DISCUSSION

The lung is the most common primary site in patients with carcinomatous involvement of the pleura.[2] Pleural involvement by lung cancer can take several forms. However, diffuse involvement of a tumor that extends to the entire surface of the lung is quite rare.[3]

In this report, we have presented 2 autopsy-confirmed cases in which small cell lung cancer presented with marked involvement of the pleura and mimicked pleural mesothelioma on diagnostic imaging. Harwood et al. termed lung cancer with marked extension to the pleura and little parenchymal involvement "pseudomesotheliomatous" carcinoma.[1] However, all cases termed pseudomesotheliomatous carcinoma in their report were in fact adenocarcinomas. Small cell lung cancer that presents with this type of progression is quite rare; to our knowledge, there have been only 2 reports in the Japanese literature.[4,5]

Small cell lung cancer is thought to originate from neuroendocrine cells. The neuroendocrine cells in the lung are mainly present near the basement membranes of the bronchial glands and their ducts.[6,7] Neuroendocrine cells are more common in the central bronchi than in peripheral bronchi,[6] and are not thought to be present in the pleura.[5] These findings suggest that small cell lung cancer does not usually originate from the pleura itself, although there have been a few reports of small cell lung cancer arising from the pleura.[8,9]

In addition, pulmonary and bronchial arteries feed the pleura, and the venous flow from the pleura returns via the pulmonary vein, while lymphatic flow returns toward the hilus via the lymphatic duct. These findings also suggest that lung cancer does not usually progress diffusely to the pleura against the direction of pulmonary blood and lymphatic flow even when marked hilar and mediastinal lymphadenopathy is present. Indeed, such lymphadenopathy is frequently observed in small cell lung cancer.

Concerning the process of diffuse pleural involvement by tumor, Harwood et al. speculated that fibrous thickening of the pleura, resulting from any of several causes, might have existed prior to the development of lung cancer, and that the lung cancer might have spread rapidly across the thickened pleura in the early stage of carcinogenesis.[1] In our case 2, no primary lesion was found, even on postmortem examination. The primary lesion might have been obliterated as a result of tumor-related pleural thickening. However, in our case 1, the process of diffuse pleural involvement could not be explained by the hypothesis proposed by Harwood et al., since the primary lesion was separate from the pleural thickening, and since there was no preexisting pleural thickening, except in the apices bilaterally, as noted on previous chest roentgenograms. We have no clear explanation for the process of diffuse pleural involvement by tumor in our case 1. However, we speculate that tumor cells in the pulmonary and/or bronchial arteries might have seeded the visceral pleura, and that the cells that took root in the pleura might have spread in an unusual fashion along the pleural space.

In making the pathologic diagnosis of mesothelioma, there are 2 major problems: 1) it is necessary to differentiate mesothelioma from lung cancer including

metastatic carcinomas; and 2) it is necessary to differentiate mesothelioma from mesothelial hyperplasia. However, it is, in general, easy to distinguish mesothelioma from small cell lung cancer, if tissue sufficient for diagnosis is obtained. In our case 2, a needle biopsy sample of the pleura showed mesothelial hyperplasia. Mesothelial cells commonly react to pleural injury by proliferating–occasionally with features suggestive of neoplasia.[10] In cases of diffuse pleural thickening, small tissue fragments are insufficient to establish the diagnosis of mesothelioma. Thoracoscopy is considered useful for the diagnosis of this tumor.

In conclusion, we have presented 2 cases in which small cell lung cancer presented an unusual pattern of progression that mimicked malignant pleural mesothelioma on diagnostic imaging. For patients with diffuse pleural thickening and effusion, the possibility of small cell lung cancer should thus be considered.

REFERENCES

1. Harwood TR, Gracey DR, Yokoo H. Pseudomesotheliomatous carcinoma of the lung: a variant of peripheral lung cancer. Am J Clin Pathol 1976;65:159–167.
2. Chernow B, Sahn SA. Carcinomatous involvement of the pleura: an analysis of 96 patients. Am J Med 1977;63:695–702.
3. Fraser RS, Peter Paré JA, Fraser RG, Paré PD. Neoplastic disease of the lungs. In: Fraser RS, Peter Paré JA, Fraser RG, Paré PD (eds) Synopsis of diseases of the chest. 2nd ed. Philadelphia: WB Saunders, 1994:445–538.
4. Tanimura A, Nakajima N, Osa T, Takeda H, Tajiri M, Iguchi Y, Tanimura Y. Primary lung cancer simulating pleural mesothelioma (in Japanese). Jpn J Chest Dis 1977;36:936–939.
5. Nomura M, Fujimura M, Matsuda T, Nakamura Y, Takayanagi N, Kitagawa M. Small cell carcinoma of the lung resembling pleural mesothelioma (in Japanese). Jpn J Lung Cancer 1994;34:1075–1078.
6. Breeze RG, Wheeldon EB. The cells of the pulmonary airways: state of the art. Am Rev Respir Dis 1977;116:705–777.
7. Gosney JR, Sissons MCJ, O'Malley JA. Quantitative study of endocrine cells immunoreactive for calcitonin in the normal adult human lung. Thorax 1985;40:866–869.
8. Boubier DP, Bell B. Small cell carcinoma of the pleura. South Med J 1989;82:1437–1438.
9. Schinkewitch PH, Gasser B, Wihlm JM, Pauli G, Quoix E. Small cell carcinoma of the pleura: a case report. Lung Cancer 1996;16:87–94.
10. Fraser RS, Peter Paré JA, Fraser RG, Paré PD. The pleura. In: Fraser RS, Peter Paré JA, Fraser RG, Paré PD (eds) Synopsis of diseases of the chest. 2nd ed. Philadelphia: WB Saunders Company, 1994:868–895.