—Case Reports—

Local Recurrence of Lung Adenocarcinoma 10 Years after Left Upper Lobectomy Resembling Pseudomesotheliomatous Adenocarcinoma: A Case Report

Junichi Okamoto[1,2], Hirotoshi Kubokura[1,2], Norio Motoda[3], Hideko Hoshina[1], Hideaki Ishii[4], Yasuhiko Kitayama[3] and Jitsuo Usuda[2]

[1]Department of Thoracic Surgery, Nippon Medical School Musashi Kosugi Hospital
[2]Department of Thoracic Surgery, Nippon Medical School
[3]Department of Pathology, Nippon Medical School Musashi Kosugi Hospital
[4]Department of Pathology, Nippon Medical School Hospital

Abstract

The form and timing of the local recurrence of lung cancer can be unpredictable and unexpected. Pseudomesotheliomatous adenocarcinoma is a rare tumor that mimics malignant pleural mesothelioma both clinically and pathologically. Distinguishing pseudomesotheliomatous adenocarcinoma from malignant pleural mesothelioma on the basis of clinical findings can be difficult; therefore, a biopsy is usually required for diagnosis. Here we report on a 73-year-old Japanese man who presented with extensive dissemination along the pleural surfaces and clinical findings similar to those of pseudomesotheliomatous lung cancer 10 years after undergoing left upper lobectomy for lung adenocarcinoma. This report provides information that will help physicians establish an accurate diagnosis in similar cases.
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Key words: pseudomesotheliomatous carcinoma, good prognosis, recurrence

Introduction

The form and timing of the local recurrence of lung cancer can be unpredictable and unexpected.

Pseudomesotheliomatous adenocarcinoma (PMAC) was first reported by Harwood et al. in 1976 in a case of lung cancer with pleural extension[1]. A diffuse pleurotropic growth pattern is common in patients with malignant mesothelioma, and a number of mesotheliomatous neoplasms demonstrating diffuse growth patterns have been described as pseudomesotheliomas[2]. In some cases, pseudomesothelioma cannot be distinguished from mesothelioma on the basis of chest radiographs or chest computed tomography (CT) scans. Even cytologic examination of pleural effusion is typically negative. Therefore, video-assisted thoracic surgery (VATS) biopsy is occasionally necessary to confirm the diagnosis.

Here we present an unusual case of lung adenocarcinoma that recurred locally with extensive

Correspondence to Junichi Okamoto, MD, PhD, Department of Thoracic Surgery, Nippon Medical School Musashi Kosugi Hospital, 1–396 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211–8533, Japan
E-mail: s3021@nms.ac.jp
Journal Website (http://www.nms.ac.jp/jnms/)

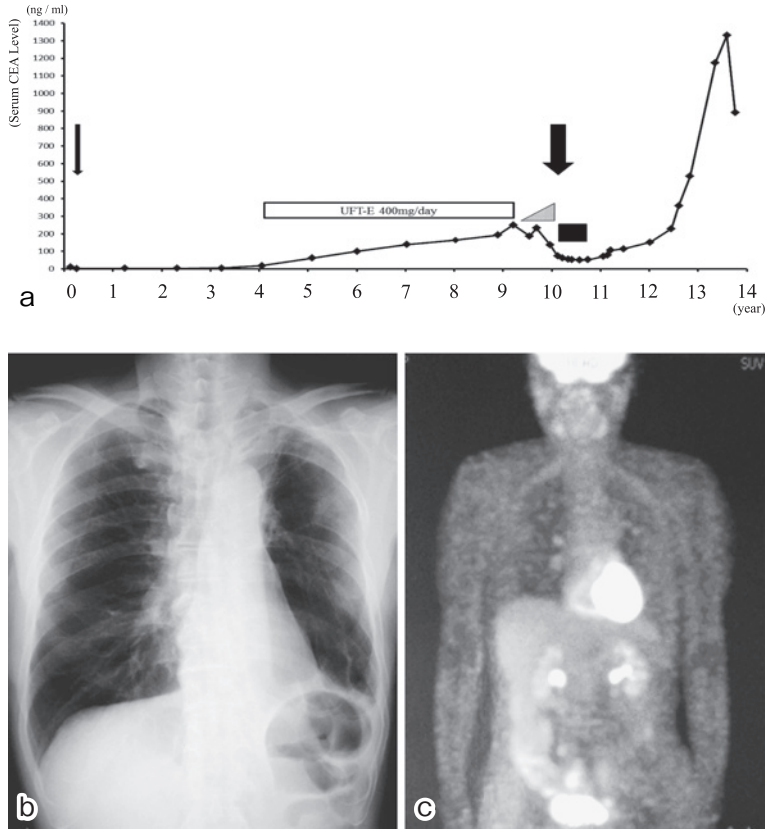

Fig. 1 There was no evidence of metastasis or other malignancy, except for an elevated serum level of carcinoembryonic antigen (CEA)
(a) The CEA level remained elevated for 5 years. The thin arrow indicates the day of the first surgery (left upper lobectomy). The thick arrow indicates the day of video-assisted thoracoscopic surgery (VATS) biopsy (second surgery). The triangle indicates pleural effusion. The solid square indicates the period of platinum doublet chemotherapy (Carboplatin+Paclitaxel).
(b) Chest radiograph obtained 10 months before biopsy.
(c) Positron emission tomography (PET) obtained 4 months before biopsy.

dissemination along the pleural surfaces and with clinical findings similar to those of pseudomesotheliomatous lung cancer 10 years after left upper lobectomy. This report should aid physicians in establishing an accurate diagnosis in similar cases.

Case Report

A 73-year-old Japanese man who had worked in the construction industry and had a history of asbestos exposure but had never smoked was being followed up after undergoing left upper lobectomy for lung adenocarcinoma. The pathological stage of the initial tumor was pT1bN0M0. Four years after surgery, the serum level of carcinoembryonic antigen (CEA) was found to be elevated. Therefore, treatment with the anticancer agent enteric-coated tegafur/uracil (UFT-E), 400 mg/day, was started and continued for 5 years. Although the serum CEA levels remained elevated for 6 years **(Fig. 1a)**, several whole-body examinations, including positron emission tomography (PET)/CT and chest CT, showed no evidence of metastasis or other malignancy **(Fig. 1b, 1c)**. Five years after the serum level of CEA was found to be elevated, UFT-E therapy was discontinued; chest radiography and CT during follow-up revealed left-sided pleural effusion and diffuse pleural thickening **(Fig. 2a, 2b)**. Cytologic examination of a sample of the pleural

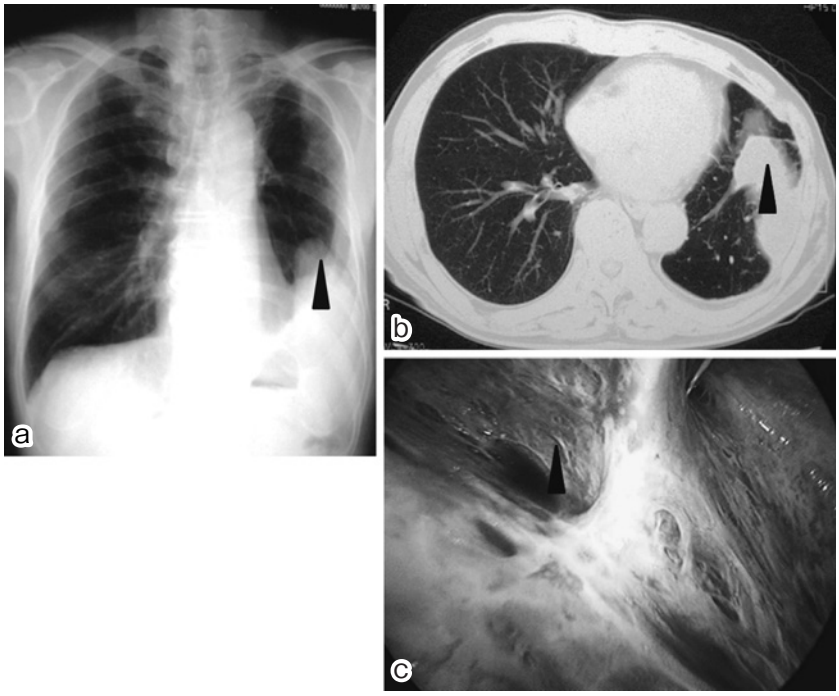

Fig. 2 (a) Chest radiography and (b) computed tomography (CT) showed left-sided pleural effusion and diffuse pleural thickening before video-assisted thoracoscopic surgery (VATS) biopsy (second operation).
(c) Intraoperative observation showed diffuse pleural thickening without evidence of a solid tumor. (**Arrows** indicate same areas.)

effusion showed blood and malignant cells and suggested adenocarcinoma. However, because the clinical findings were consistent with both PMAC-like recurrence and malignant mesothelioma, a surgical biopsy was performed to obtain a more definitive histopathological diagnosis.

After a combination of general and epidural anesthesia was induced, a double-lumen endotracheal tube was inserted, and the patient was placed in the lateral decubitus position. An 8-cm skin incision was made in the sixth intercostal space, and a trocar-port was created in at the seventh intercostal space; then, VATS was performed to collect tumor samples. The tumor, which had spread across the visceral and parietal pleura, resembled a malignant mesothelioma (**Fig. 2c**). Two specimens of parietal pleura were collected with ultrasonic coagulating shears.

Macroscopic examination identified the primary tumor in the periphery of the left upper lobe (S^4) with a pleural indentation measuring 2.5×1.3 cm. Microscopic examination showed that the tumor consisted of atypical cuboidal cells with hyperchromatic nuclei and prominent nucleoli, forming cribriform and papillary patterns, with mucin production. No pleural infiltration was observed. Invasive adenocarcinoma of mixed subtype (papillary predominant), pT1bN0M0-stage IA, was diagnosed (**Fig. 3a**).

Pathological analysis of the pleural biopsy specimen showed mucin-producing atypical cuboidal cells that had infiltrated the parietal pleura (**Fig. 3b**). Staining with Alcian blue and periodic acid-Schiff confirmed the presence of mucin, and some tumor cells were evident (data not shown). The tumor cells were immunohistochemically positive for cytokeratin (CK) 7 (**Fig. 3c**), CEA (**Fig. 3d**), napsin A (**Fig. 3e**), and surfactant apoprotein but were negative for calretinin, D2-40, CK5/6, and CK20 (data not shown). The immunohistochemical profile and morphological similarities led to a final diagnosis of metastatic adenocarcinoma consistent with recurrence of lung cancer.

The patient was given 4 cycles of platinum doublet chemotherapy comprising carboplatin and paclitaxel and was followed-up for 2 years, after

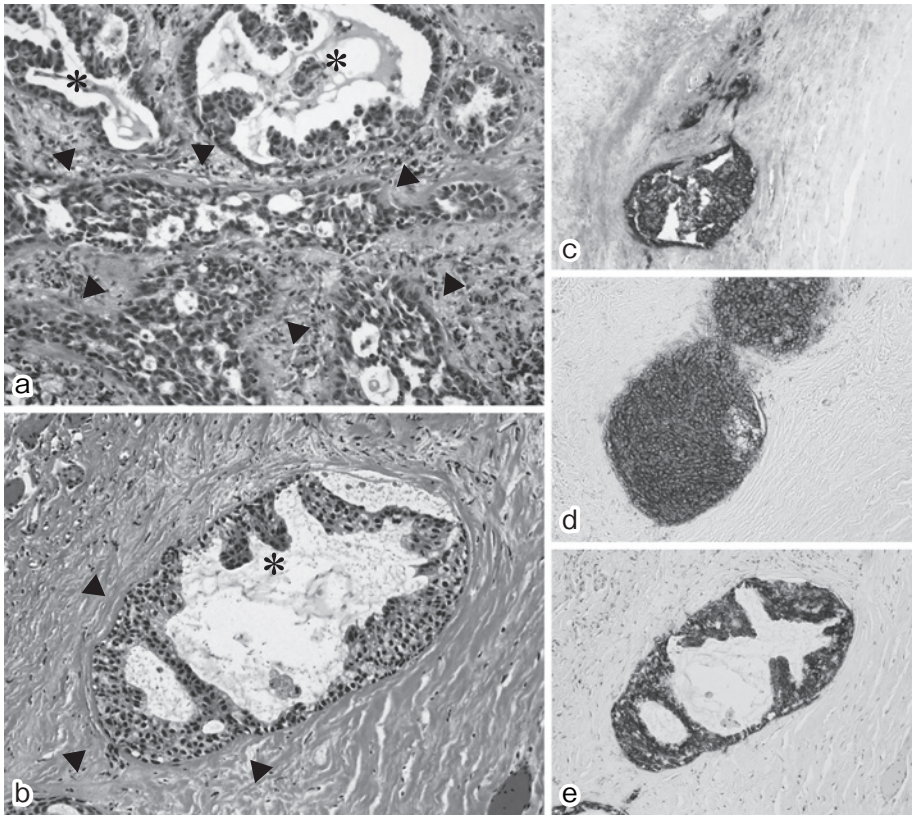

Fig. 3 Histopathological examination (hematoxylin and eosin stain) showed similar features in both primary lung tumor (a) and local pleural recurrence (b). Cribriform patterns **(arrowheads)** and papillary **(asterisks)** patterns were observed, with mucin production. Immunohistochemical examination of the pleural tumor was performed. Tumor cells were positive for (c) CK7, (d) CEA, and (e) napsin A.

which recurrence was discovered. He eventually died of metastasis to the brain and multiple locations in the lungs.

Discussion and Conclusion

PMAC is a rare variant of peripheral adenocarcinoma of the lung and is characterized by clinical, radiological, and pathological features similar to those of malignant mesothelioma[3]. The present case was extremely unusual because of local recurrence mimicking PMAC. Our search of the literature yielded no similar cases. The diagnosis of PMAC is usually based on histochemical, immunohistochemical, and ultrastructural findings[3]. Patients with PMAC are typically heavy smokers with a history of exposure to asbestos, iron, or both[4]. In the present case, pleural metastases of lung adenocarcinoma appeared as solid tumors of variable thickness that resembled malignant mesothelioma[5]. The clinical presentation was not PMAC but was similar to PMAC. Furthermore, distinguishing between metastases from adenocarcinoma and mesothelioma is extremely difficult[5]. In the present patient, no solid lung tumor or pleural effusion was initially present in the thoracic cavity, even though serum CEA levels remained persistently elevated. Furthermore, PET/CT showed no evidence of metastasis. However, pleural effusion appeared at a later stage. The most common radiographic finding of PMAC is pleural effusion with or without pleural masses[6], similar to the finding of malignant mesothelioma. These symptoms were apparent in our patient.

The question was why in our case, local recurrence was on the pleura, mimicking PMAC. Liu et al. have reported evidence of permeation of tumor cells in the cisterns into the pleural cavity via

adjacent stomas in the pulmonary ligament. The pulmonary ligament was found to have numerous lymphatic cisterns with stomas in the thoracic cavity[7]. Thus, tumor invasion into the subpleural lymphatics might be required for the development of pleural carcinomatosis.

Our patient presented with p-stage IA disease that recurred locally 10 years after lobectomy and resembled PMAC. After local recurrence was diagnosed, the patient was given 4 cycles of platinum doublet chemotherapy comprising carboplatin and paclitaxel and was followed-up for 2 years. Kelsey et al. have reported that the risk of local disease recurrence after surgery in patients with stage I to II non-small cell lung cancer (NSCLC) was 23% within 5 years[8]. The patients studied by Kelsey et al. included those with stage II disease; however, for patients with stage I, the recurrence rate was less than 23%[8]. The 5-year survival rates of patients with newly classified T1 disease were 90.3% for T1aN0M0 and 81.5% for T1bN0M0[9]. Okada et al. have reported that the 5-year survival rates for patients with c-stage I NSCLC and normal and high preoperative CEA levels were 75.2% and 53.8%, respectively, and that this difference was significant[10]. Furthermore, Maeda et al. have reported that the probabilities of recurrence-free status at 3 and 5 years from the point of 5 years after primary tumor resection were 92% and 87%, respectively. For patients with CEA levels within the normal range and those with elevated CEA levels, the probabilities of recurrence-free status were 88.6% and 81.4%, respectively[11]. On the other hand, pleural pseudomesotheliomatous tumors typically have a poor prognosis, with a median survival of only 8 months, which is similar to that of stage IV NSCLC[12]. Although the case reported here resembled PMAC in appearance, the prognosis of our patient was more similar to that of patients with elevated CEA and c-stage I NSCLC rather than to that reported for previous patients with PMAC[4,12,13].

Our patient received long-term treatment with UFT. Abe et al. have reported on a patient who achieved long-term survival after recurrent adrenal metastasis of lung cancer was treated with long-term UFT therapy[14]. Taken together, the long-term survival of our patient might be attributed to his being a nonsmoker and having received UFT-E or platinum doublet chemotherapy.

In conclusion, we have presented a case of lung adenocarcinoma that recurred as locally PMAC with extensive dissemination along the pleural surfaces 10 years after left upper lobectomy. This case report emphasizes that even if surgery was performed many years earlier, PMAC-like local recurrence and additional therapy should be considered if serum CEA levels are elevated.

Conflict of Interest: The authors report no conflicts of interest.

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. Attanoos RL, Gibbs AR: 'Pseudomesotheliomatous' carcinomas of the pleura: a 10-years analysis of cases from the environmental lung disease research group, Cardiff. Histopathology 2003; 43: 444–452.
3. Attems JH, Lintner F: Pseudomesotheliomatous adenocarcinoma of the lung with rhabdoid features. Pathol Res Pract 2001; 197: 841–846.
4. Mizuoka H, Uemura Y, Nakagawa H, et al.: Pseudomesotheliomatous carcinoma of the lung- an autopsy. Jpn J Cancer Clin 2000; 46: 89–96 (In Japanese).
5. Oka K, Otani S, Yoshimura T, et al.: Mucin-negative pseudomesotheliomatous adenocarcinoma of the lung. Report of three cases. Acta Oncologica 1999; 38: 1119–1121.
6. Shah IA, Salvatore JR, Kummet T, Gani OS, Wheeler LA: Pseudomesotheliomatous carcinoma involving pleura and peritoneum: a clinicopathologic and immunohistochemical study of three cases. Ann Diag Pathol 1999; 3: 148–159.
7. Liu S, Oshiro H, Kato Y, Kudo M, Ebihara Y: The Role of the Pulmonary Ligament in the Pathogenesis of Pleural Carcinomatosis. Japanese Journal of lung cancer 2001; 41: 643–648 (In Japanese).
8. Kelsey CR, Marks LB, Hollis D, et al.: Local recurrence after surgery for early stage lung cancer. An 11-year experience with 975 patients. Cancer 2009; 115: 5218–5227.
9. Suzuki M, Yoshida S, Tamura H, et al.: Applicability of the revised International Association for the Study of Lung Cancer staging system to operable non-small-cell lung cancers. Eur J Cardiothorac Surg 2009; 36: 1031–1036.
10. Okada M, Nishio W, Sakamoto T, et al.: Prognostic significance of perioperative serum carcinoembryonic antigen in non-small cell lung cancer: analysis of 1000 consecutive resections for

clinical stage I disease. Ann Thorac Surg 2004; 78: 216–221.
11. Maeda R, Yoshida J, Hishida T, et al.: Late recurrence of non-small cell lung cancer more than 5 years after complete resection: incidence and clinical implications in patient follow-up. Chest 2010; 138: 145–150.
12. Snaebjornsson P, Vos CG, Hartemink KJ, et al.: Fetal hemothorax caused by pseudomesotheliomatous carcinoma of the lung. Patholog Res Int 2011; 836054. doi: 10.4061/2011/836054. Epub 2011, Jun 27.
13. Tambo Y, Kita T, Kibe Y, Kasahara K, Fujimura M, Nakao S : An autopsy case of pseudomesotheliomatous adenocarcinoma of the lung. Japanese Journal of lung cancer 2006; 46: 145–150 (In Japanese).
14. Abe N, Yamada N, Ishihara T, Kohiyama R: A long-term surviving case of recurrent adrenal metastasis of lung cancer treated by Uracil-Tegafur. Japanese Journal of lung cancer 2006; 46: 161–165 (In Japanese).

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