

A Case of T0 Small Cell Lung Cancer

Ryoji Kawano¹; Enjo Hata¹; Shingo Ikeda¹;
Toshiya Yokota¹; Shin Karita¹; Kazuyoshi Tamaki¹

ABSTRACT **Background.** Lung cancer rarely shows a lymph node metastasis to pulmonary hilar and/or mediastinal regions without the primary site of the lung being unable to be detected. **Case.** A 68-year-old man demonstrated a right abnormal hilar shadow on a chest X-ray film. A computed tomography (CT) revealed an enlarged mass at the right pulmonary hilar node, and this mass was diagnosed to be poorly differentiated carcinoma by transbronchial aspiration cytology. However, no primary lesion in the lung was apparent, and the extrathoracic findings showed no abnormalities despite a thorough examination. We thus performed a tumorectomy with right upper lobectomy and mediastinal nodal dissection because of the possibility of a lung origin based on the lymphatic routes to the tumor. The microscopical and immunohistochemical findings were consistent with small cell carcinoma in the pulmonary hilar node. Although no primary lesion of the resected lobe and also other lobes of the lung was found despite detailed examinations, positive immunoreactivity against anti-thyroid transcription factor-1 (TTF-1) antibody revealed this tumor to have originated in the lung. Therefore, we consider that this patient is a rare case of primary unknown T0 lung cancer with metastasis in the pulmonary hilar lymph node. **Conclusions.** In case of T0 lung cancer, since the primary lesion may later be identified, a strict follow-up study after the operation is necessary. (*JJLC*. 2005;45:377-380)

KEY WORDS T0 lung cancer, Small cell carcinoma, Thyroid transcription factor-1 (TTF-1), Lymph node metastasis, Cancer of unknown primary site

INTRODUCTION

Lung cancer often shows lymph node metastasis in the pulmonary hilar or mediastinal regions during the early stage. Occasionally, the metastatic site is clinically found prior to the detection of the primary lesion of the lung. We present a rare case with primary-unknown small cell carcinoma appearing in the pulmonary hilar node. Immunohistochemical analysis was helpful in estimating the primary site. Since the first case of primary-unknown small cell carcinoma reported by Suemasu et al¹ was described, the number of such T0 lung cancer cases in Japan, as far as we know, is less than 10.

CASE

A 68-year-old man demonstrated an abnormal shadow in the right pulmonary hilar region on a chest X-ray examination during a routine medical checkup (Figure 1). He had smoked 40 cigarettes a day for 40 years, but his past



Figure 1. Chest X-ray film shows the right pulmonary hilar shadow.

medical history and physical examinations showed no abnormalities. The laboratory blood test profile was normal except for a slightly elevated neuron specific enolase (NSE) of 11 ng/ml (normal range < 10 ng/ml). A CT

¹Surgical Department of Respiratory Center, Mitsui Memorial Hospital, Japan.

Reprints: Ryoji Kawano, Surgical Department of Respiratory Center, Mitsui Memorial Hospital, 1 Kandaizumicho, Chiyoda-ku, Tokyo

101-8643, Japan (e-mail: r-kawa@mitsuihosp.or.jp)

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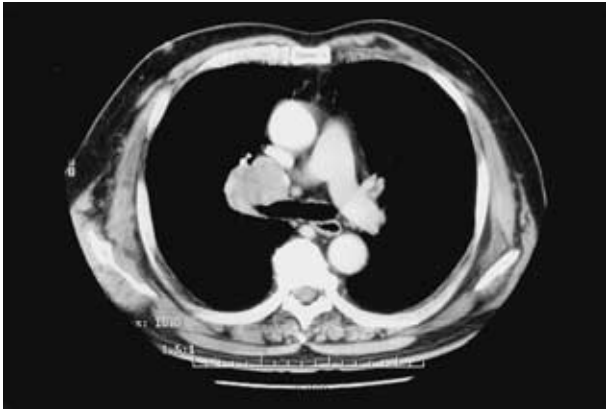


Figure 2. CT shows the tumor to be located in the pulmonary hilar region without apparent invasion to the surrounding structures.

scan of the thorax identified a homogenous round mass measuring 5.5-cm size in the right pulmonary hilar region. The CT showed the mass to be located in the region adjacent to the azygos vein, right main bronchus, right upper lobe bronchus, right pulmonary artery and its branches (Figure 2). However, no abnormal CT findings were found in the bilateral lung fields, except for an emphysematous lung. Bronchoscopy showed slight erythema on the lateral side in the right main bronchus and the upper and anterior wall of the right upper lobe bronchus. In addition, no endoluminal mucosal abnormality was present. However, the right B³ orifice was constricted due to an extrinsic mass. Brushing cytology of all bronchopulmonary segments of the right upper lobe bronchus was performed, but no significant findings were obtained. Transbronchial aspiration cytology (TBAC) was done at the right main bronchus. TBAC revealed the mass to consist of epithelial tumor cells with poor differentiation. No evidence of malignancy was seen in the systemic examinations of the brain, bones, or abdomen. A slight degree of mediastinal lymphadenopathy was noted in the pretracheal region. Pulmonary arteriography showed striking encasement of each branch of the right upper pulmonary artery. However, no evident filling defect or wall irregularity of the main stem or upper lobe branches of the right pulmonary artery could be seen, and the blood flow was well preserved. From the results of these unique locoregional findings, the presumptive diagnosis was a poorly differentiated carcinoma originating in the right upper lobe with involvement of a hilar lymph node. We therefore performed a right thoracotomy through the me-

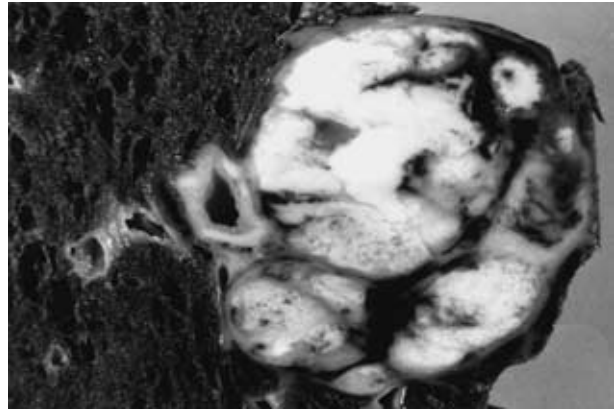


Figure 3. The tumor cut surface is grayish white, anthracotic, firm, and shows extensive necrosis.

dian sternotomy because of the possibility of tumor invasion to the vessels and right main bronchus. An exploration of the thoracic cavity and lung showed no abnormalities. The tumor was located closely to the right pulmonary hilar region, and was firmly fixed to the mediastinal surface of the right upper lobe, however, the tumor could be released from the right main bronchus, and from each branch of the upper pulmonary artery. There was no true invasion of these structures. Since the possibility remained that primary lung cancer originating in the right upper lobe had metastasized to the pulmonary hilar node, we performed a right upper lobectomy with mediastinal nodal dissection. The patient tolerated the operation well and was discharged without complications.

The tumor measured 5.0 × 4.0 × 3.2 cm in size with no correlation to the bronchi in the right upper lobe, and it was located in a region which is consistent with the right upper lobe lymph node. The cut surface of the tumor was grayish white, anthracotic, firm, and showed extensive necrosis (Figure 3) No tumor was found in the right upper lobe despite performing further examinations of lung tissue sectioned 3 mm in thickness. The tumor was composed of small atypical cells with a round to fusiform shape, and scant cytoplasm. They formed nests, streams, and ribbons. Mitosis was frequent in tumor cells. Occasionally, large tumor cells with bizarre nuclei were observed (Figure 4A) The tumor cells showed positive immunoreactivities for antibodies of NSE, neural cell adhesion molecule(N-CAM), and thyroid transcription factor-1 (TTF-1)(Figure 4B) Furthermore, normal histological configuration of the lymph node was seen at the periph-

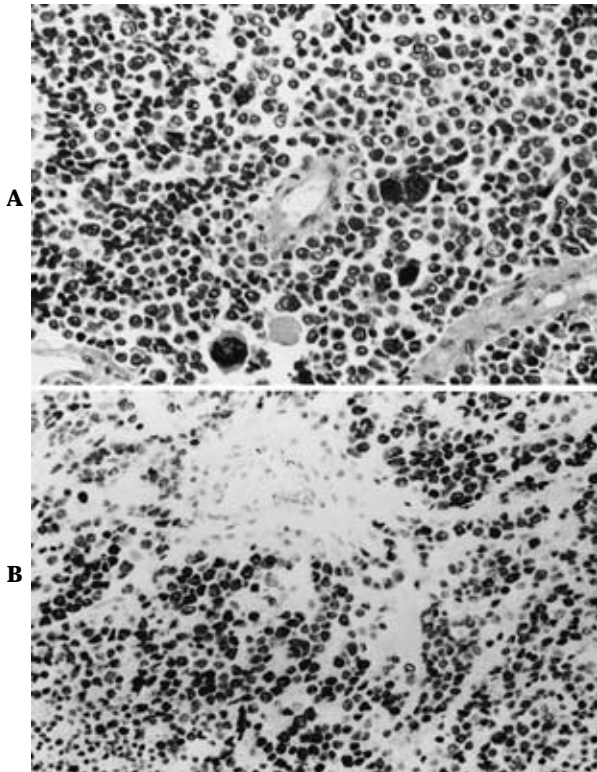


Figure 4. **A.** The tumor was composed of small atypical cells with a round to fusiform shape, and scant cytoplasm. The mitotic rate is high. **B.** Positive immunoreaction for anti TTF-1 antibody is seen in the nuclei of tumor cells.

eral region of the tumor. Therefore, the final diagnosis of this tumor was small cell carcinoma which derived from lung parenchyma. The tumor did not invade the visceral pleura of the resected upper lobe, and no tumor involvement with the other nodes was seen. The patient was discharged without any complications, and then adjuvant chemotherapy was performed. No tumor was recognized during the 20-month postoperative period.

DISCUSSION

If an epithelial tumor is found in the pulmonary hilar or mediastinal nodes alone, then several speculations about tumorigenesis are possible. First, metastatic carcinoma to these nodes from some unknown primary site should be considered. Metastatic carcinoma to the thoracic lymph nodes without detection of the primary site is rare and has seldom been reported.² T0 lung cancer, based on the general rules for the clinical and pathological records of lung cancer,³ is also included in the classification of intrathoracic tumors with an unknown primary

site. Only when the histogenesis of tumor cells originating from lung tissue is known, can they be diagnosed as T0 lung cancer cases. Some possible reasons for lack of detection of the primary site were that the tumor size of the primary lesion was not large enough to be evident, or that the tumor spontaneously regressed. However, the clinical course and biological behavior of the present tumor has not yet been clarified.

Second, primary carcinoma may arise from endogenous cells present within the affected pulmonary hilar or mediastinal lymph node.⁴ In fact, gland inclusions from which epithelial tumor originates within the lymph node have been previously reported.⁵ However, no evidence of this event has yet been confirmed. Therefore, further pathological study is required. The origin of this tumor may indeed be the lung tissue, because its morphologic and histologic aspects were compatible with a pulmonary origin, and the lymphatic drainage from the lung passes through these nodes. Furthermore, an immunohistochemical study may help determine the biological characteristics of the primary tumor, and its histological origin. We previously reported two cases of T0 lung cancer in which an immunohistochemical application of antibody against surfactant apoprotein on alveolar epithelial cells was a useful method for identifying a lung origin in metastatic adenocarcinoma to a lymph node.⁶ In general, it is useful for the diagnosis of lung adenocarcinoma to apply an immunohistochemical method using cytokeratin 7 and 20 antibodies,^{7,8} and surfactant apoprotein antibody, whereas there are no expressions against these immunohistochemical antibodies in small cell lung cancer. Small cell carcinoma of the lymph node originating from the lung tissue could be confirmed by applying antibody against TTF-1. This antibody has a specific immunoreactivity for the lung and thyroid epithelial cells and their tumors.^{9,10} Therefore, it is a very useful marker in the diagnosis of tumors of lung origin. However, small cell carcinoma arising from the urinary bladder and pancreas occasionally shows positive immunoreactions, but no abnormal findings of these organs were demonstrated in the present case. The complementary use of immunohistochemical markers showed findings consistent with small cell carcinoma of the lung.

Regarding the treatment of such cases, since the lung is regarded as the primary site of metastasis to the lymph nodes, as mentioned above, a lung resection with lymph node dissection is indicated. Surgical treatment is neces-

sary because the drainage routes flow from the primary lobe to the region of tumor. If a primary lesion cannot be detected, then the second operation may be needed at the point when the primary lesion would appear.

Finally, in cases of unknown primary site of lung cancer, since the primary lesion may later be identified, a strict follow-up study after the operation is necessary.⁶

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