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An Adenocarcinoma of Lung with Unusual Very Slow Growth
—A case report—

The prognosis of lung cancer is very poor. Patients with lung cancer have usually no symptom in early stage or some mild cough, sputum. When patient feel weight loss or dyspnea, majority of patients with lung cancer are advanced stage and inoperable. The growth rate of lung cancer is different according to cell type of tumor and related to prognosis. Generally, tumor doubling time (TDT) of lung cancer has been known that small cell lung cancer is about 65 days, squamous cell carcinoma is about 90 days, and adenocarcinoma is about 185 days. There has been rarely reported of lung cancer with very fast or very slow growth. The prognosis of a slow growing lung cancer is relatively good but rapidly growing cancer is not. We report a very rare case that surgically treated early stage non-small cell lung cancer (adenocarcinoma) with 4-year-TDT without invasion or distant metastasis. **(J Lung Cancer 2006;5(1):51—54)**

Key Words: Tumor doubling time, Slow growth, Lung cancer, Adenocarcinoma

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Adenocarcinoma is the most common histologic type of lung cancer in many countries, and its incidence has increased over the last 30 years. Most patients with early-stage adenocarcinoma are asymptomatic and the common initial finding is of a peripheral nodule detected during routine radiographic examinations. Some peripheral lung nodule of adenocarcinoma is relatively slow growing. Recently, we have experienced a very rare multiseptated cystic adenocarcinoma of lung that showed extremely slow growth. Tumor doubling time (TDT) was about 4 years and there was no metastasis during 8 years. Adenocarcinoma of lung was so early stage that treated by lobectomy. Four years is the longest time of TDT of lung cancer, as far as we know.

CASE REPORT

Eight years ago a 69-year-old woman sought medical attention because of mild cough. Simple radiography and a computed tomographic (CT) scan (Fig. 1) of the chest revealed a pulmonary nodule, sized about 2.8×1.7 cm, in the superior segment of the right lower lobe with a well-marginated multiseptated cavity. She was recommended for biopsy, but she refused further evaluation and wanted treatment of symptoms only. Subsequently, she felt cough intermittently and underwent a chest X-ray 2 years later. The mass was found to have grown to 4×3.2×2.2 cm (Fig. 2). She was recommended for biopsy once more, but continued to refuse an invasive study. 6 years later (eight years after her initial presentation), she revisited our

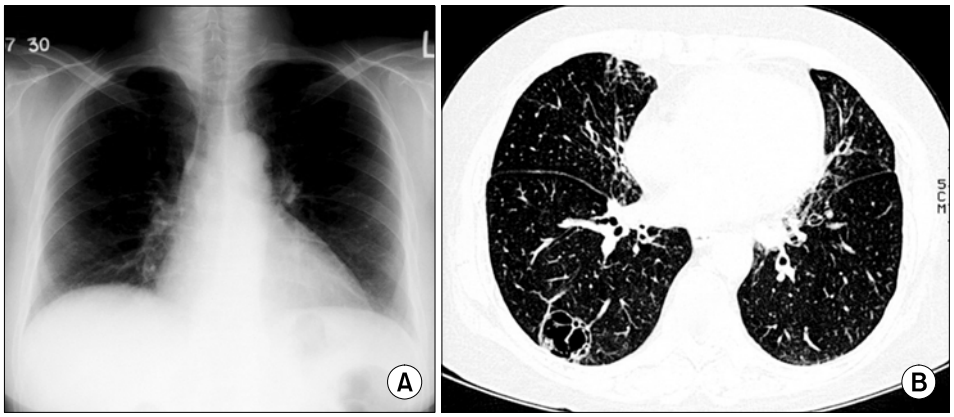

Fig. 1. Chest radiography (A) and HRCT scan (B) at initial presentation, demonstrating a well-defined multi-septated cavitary lung lesion in the superior segment of the right lower lobe.

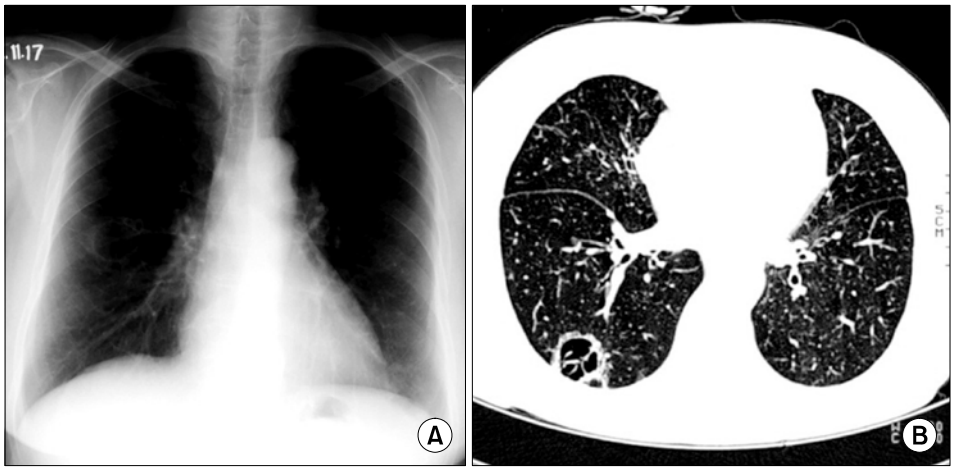

Fig. 2. Chest radiography (A) and HRCT scan (B) taken 2 years later, demonstrating that the size of lung mass had increased slightly.

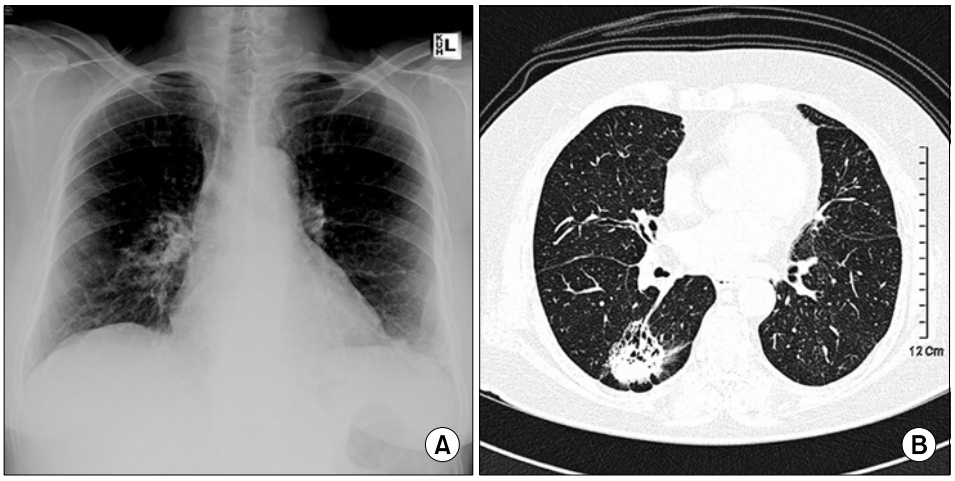

Fig. 3. Chest radiography (A) and HRCT scan (B) taken 8 years after the initial presentation showing that the cavitary lung mass had increased in size and developed a solid portion.

hospital because of a dry cough. She had a 30-year smoking history, although she had quit some 9 years previously. Her vital signs were stable and cervical lymphadenopathy was not observed. Her breathing sounds were clear without crackle or wheezing. Arterial oxygen saturation was 98 percent while the patient was breathing ambient air. Complete blood counts and blood chemistry were normal and an electrocardiogram revealed a normal sinus rhythm. Chest radiography and a CT scan (Fig. 3) showed a non-calcified mass, measured up to 4.7×4×4 cm in the right lower lung field. As compared with the findings

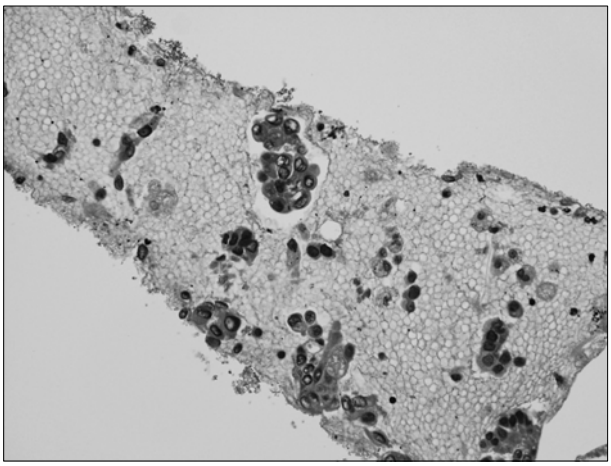

Fig. 4. Percutaneous transthoracic needle aspiration of lung. Hematoxylin and Eosin (H&E) stain (×400). The cell-block slide showed a few clusters of atypical cells with irregular nuclei and moderate amounts of cytoplasm, suggestive of adenocarcinoma.

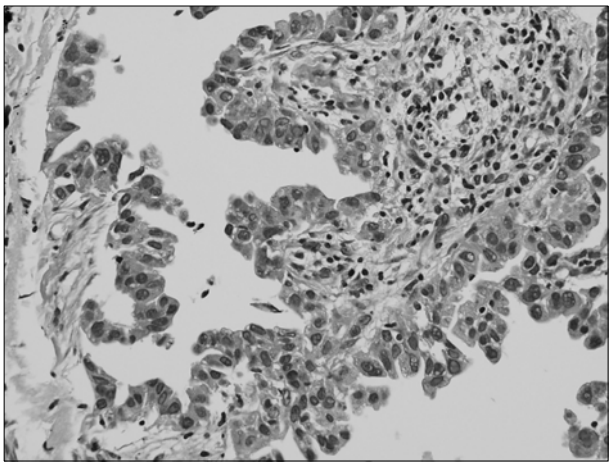

Fig. 6. Well differentiated adenocarcinoma of the lung, showing a bronchioloalveolar carcinoma-like growth pattern with atypical cells lining the alveolar wall (H&E stain, ×400).

Fig. 5. Gross finding of lung cancer in the right lower lobe, during lobectomy.

obtained 8 years previously, the mass had enlarged and developed a solid portion. On this occasion she consented to biopsy. The pathologic finding by percutaneus transthoracic needle aspiration was non small cell lung cancer (adenocarcinoma) (Fig. 4). The positron emission tomographic (PET) scan, conducted for lymph nodal staging, was of a focal hypermetabolic lesion (pSUV=3.14) in the superior segment of the right lower lobe without metastasis. Magnetic resonance imaging of the brain returned normal findings without a metastatic lesion. Her preoperative radiologic stage was Ib (T2N0M0) and she was referred to chest surgery for operation. Lobectomy of the right lower lobe was done (Fig. 5) and the final biopsy report was of a well differentiated adenocarcinoma with involvement of the visceral pleura by the tumor but without metastasis to the lymph nodes (0/21) of the lung. Some tumor regions showed a bronchioloalveolar cell carcinoma (BAC) like growth pattern (Fig. 6). The postoperative pathologic stage was the same as preoperative radiologic stage. Patient was discharged without postoperative sequelae. She is currently doing well and has no evidence of recurrence or metastasis at 1 year after operation.

DISCUSSION

Bronchogenic carcinomas of various cell types usually behave according to the rules imposed by cell growth kinetics. Most of lung cancers grow rapidly like other cancers, but in some cases they do not. For example, the tumor doubling time (TDT) of squamous cell carcinoma was reported to be about 90 days, small cell lung cancer about 65 days, and adenocarcinoma about 185 days and the TDT of adenocarcinoma was found to be longer than others(1). There were some reports describing slow-growing adenocarcinoma showed a TDT over 400 days up to about 1,000 days(2). On the other hand, the shortest TDT reported for squamous cell carcinoma was 7.5

days(3). We calculated the TDT of the present case, using the method described by Schwartz(4), and obtained a value of about 1,632 days (=4.5 years). Adenocarcinoma of lung in our case was resected 8 years later since discovered initially, but stage was Ib without metastasis. To our knowledge, this is the longest TDT of lung adenocarcinoma. The growth rates of lung tumors are closely related to prognosis(5) and the prognosis of a slow growing tumor is relatively good. Several studies have reported two types of peripheral adenocarcinoma of the lung by imaging study. One starts as localized ground-glass opacity on CT with slow growing pattern and the other as a solid attenuation with rapid growth(6). Localized BAC demonstrates a greater extent of ground-glass opacity (GGO) on CT scans, and has a good prognosis after treatment. In case of small sized (<3 cm in longest diameter) adenocarcinoma of lung the results are similar(7~9). Noguchi et al. classified small peripheral adenocarcinoma of the lung into six types, i.e., A-F. Types A, B, and C are adenocarcinomas showing a growth pattern that involves replacement of alveolar lining cells, whereas the other types show solid and expansive tumor growth. Patients with a type A or B tumor showed no lymph node metastasis and had an excellent prognosis with a 5-year survival rate of 100%, whereas patients with type C tumor showed a high incidence (28%) of lymph node metastasis and a poorer prognosis (5-year survival rate, 75%)(10). The tumor in our case contained both solid and BAC patterns. The most common radiologic finding in BAC is lobar or diffuse consolidation, and some cases have solitary nodules or multiple nodules(11). However, cavitation is unusual in BAC, having been reported to occur in only 7% of patients in previous reports(12) and it is suggestive invasive adenocarcinoma by the criteria of 1999 revised WHO classification of lung and pleural tumors (13). Multiseptated cysts are also extremely rare in BAC(14). The question raised by our case was that whether malignant cells had transformed from an initially observed benign cyst cell or whether malignant cells in the original cystic mass had grown very slowly over 8 years. The question is difficult to answer, though the latter is more likely because no boundary of benign cells was found around the tumor by pathologic exam and a solid cystic mass lesion was observed by CT at the initial presentation. Eight years later, the solid portion had increased gradually to fill the tumor cavity without invasion to surrounding organ and without central necrosis. Thus we describe an adenocarcinoma of lung which had extremely rare growing behavior with multiseptation and without metastasis over an 8-year period.

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