

Pleomorphic Carcinoma of the Lung in Which the Sarcomatous Element Grew Rapidly: A Case Report

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We report a case of pleomorphic carcinoma of the lung that showed a rapid growth. The patient was a 77-year-old female with an abnormality detected in her chest radiograph during a screening examination, but a definite diagnosis could not be obtained based on a needle biopsy guided by CT. After one month, the tumor had continued to grown rapidly and lung cancer was strongly suspected, so the patient underwent surgery. The intraoperative diagnosis demonstrated it to be a pleomorphic carcinoma of the lung in which a squamous element and a sarcomatous element were mixed; and a right lower lobectomy and lymphadenectomy were performed. In a pathological examination after surgery, the tumor was found to be composed of a sarcomatous element that had a high MIB-1 index of 30%, and this was believed to be the cause of the rapid growth. (Ann Thorac Cardiovasc Surg 2009; 15: 111–114)

Key words: lung cancer, pleomorphic carcinoma, MIB-1

Introduction

Pleomorphic carcinoma is a rare tumor that makes up only 0.3% to 1% of all malignant lung tumors, and its clinical prognosis is not easily understood.^{1,2)} This time, we experienced a case of pleomorphic carcinoma of the lung in which the tumor grew rapidly during the follow-up period, the cause of which was believed to be a sarcomatous element because of its MIB-1 index. We herein report our findings of this case and include bibliographical considerations.

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Case Report

A chest radiograph was taken during a screening examination of a 77-year-old female in whom an abnormality was found in the right lower lung field. A chest CT confirmed a mass measuring 50 × 30 mm in the right lung (S¹⁰). Although a bronchoscopy and CT-guided needle biopsy were performed, a definite diagnosis could not be obtained, and the patient was introduced to our department one month later. Regarding the patient's family history, her brother had rectal cancer and her sister had colon cancer. No particular abnormalities were observed in the initial examination performed upon admission. Regarding tumor markers, SCC was 4.9 ng/ml, CYFRA was 4.0 ng/ml, CEA was 3.0 ng/ml, and SLX was 26 U/ml; slight elevations of SCC and CYFRA were observed. Among the findings from the chest radiograph, a mass with an irregular margin was confirmed in the right lower field of the lung around the diaphragm. The diameter of the tumor had increased from 50 mm to 70 mm in one month (Fig. 1). On the chest CT, while the size of the tumor was 50 × 30 mm on the initial visit, it had

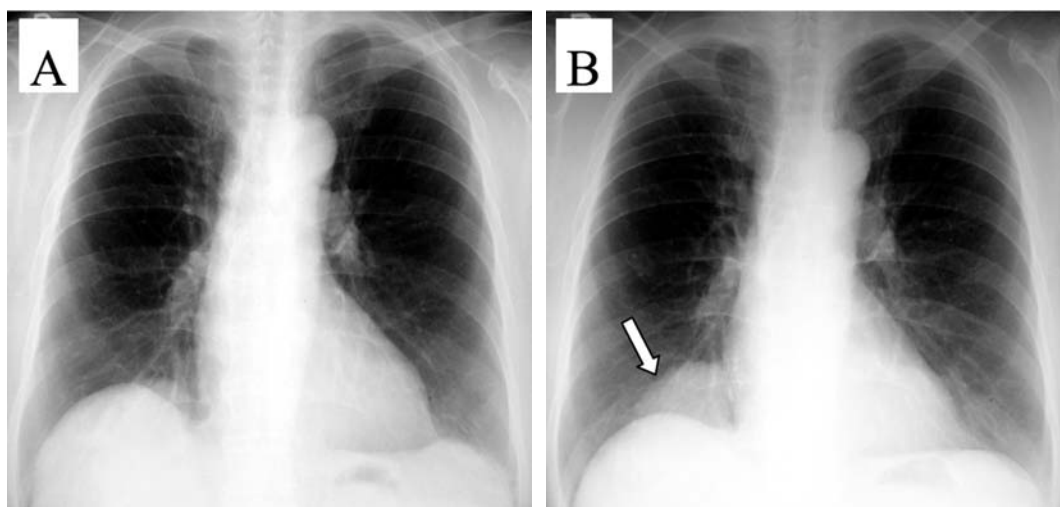


Fig. 1. Frontal chest X-ray.

A: On the first visit, a tumor measuring 50 mm was confirmed in the right lower field of the lung around the diaphragm was confirmed.

B: One month later, the tumor had become 70 mm, which showed a tendency toward rapid growth (arrow).

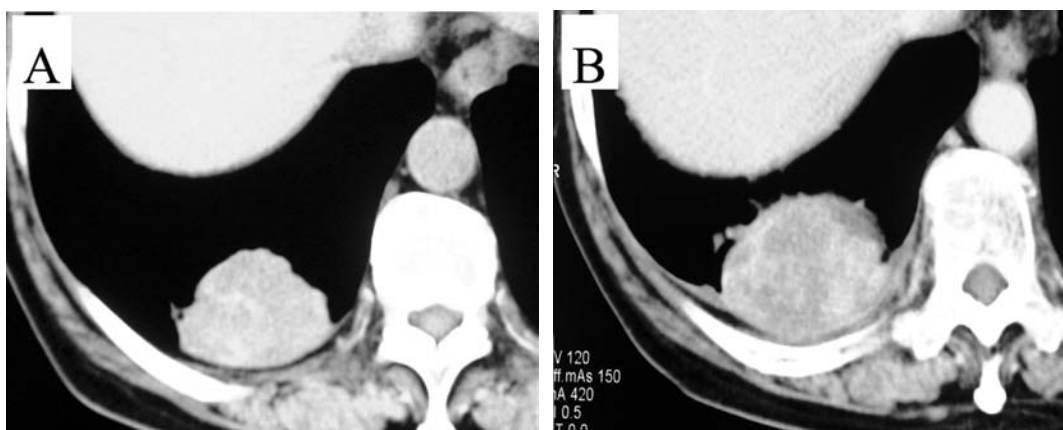


Fig. 2. Chest CT.

A: On the first visit, the size of the tumor was 50 × 30 mm.

B: One month later, the size of the tumor had increased to 65 × 50 mm, and the tumor showed a non-homogeneous internal density and an accumulation of pleural effusion.

increased to 65 × 50 mm by one month later; the CT also revealed the non-homogeneous internal density of the tumor, with a low density in the central portion. In addition there was also an accumulation of pleural effusion, and invasion into the thoracic wall or the diaphragm was also suspected (Fig. 2). Surgery was performed with a strong suspicion of lung cancer.

When a fifth intercostal thoracotomy was performed, a small amount of pleural effusion was observed in the thoracic cavity. The tumor was about the size of a child's fist, and there was no invasion into the thoracic wall or

the diaphragm; we performed a right lower lobectomy. In our intraoperative histological diagnosis, the patient was diagnosed to have a pleomorphic carcinoma in which a sarcomatous element and squamous cell carcinoma were mixed; and a mediastinal lymphadenectomy was performed. In the excised specimen, the size of the tumor was 75 × 55 × 60 mm, and the solid and necrotic areas were mixed inside the tumor. In the histopathological examination, the tumor was determined to be a pleomorphic carcinoma composed of 70% squamous cell carcinoma and 30% sarcoma consisting of spindle cells.

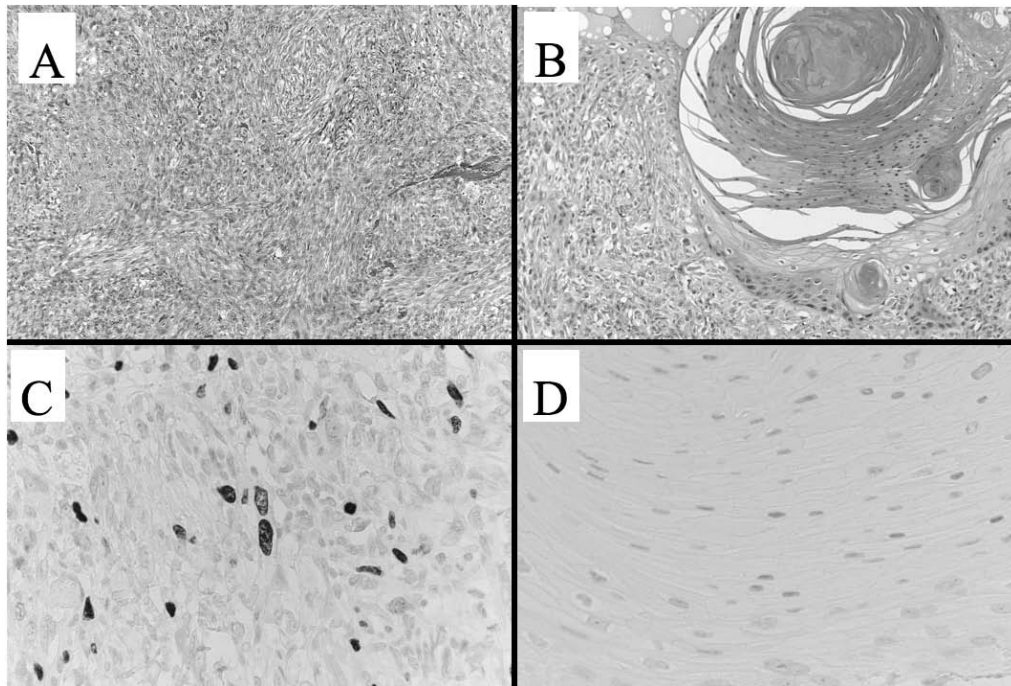


Fig. 3. Histopathological findings.

- A: Sarcomatous element. (HE stain: $\times 100$)
- B: Squamous cell carcinoma. (HE stain: $\times 100$)
- C: Sarcomatous element. (MIB-1: $\times 400$)
- D: Squamous cell carcinoma. (MIB-1: $\times 400$)

Squamous cell carcinoma made up 70% of the entire tumor; the sarcoma composed of spindle cells was 30%. In the sarcomatous element, there were no ectopic components such as bone and cartilage, muscle, or nerves. The hemorrhage and necrotic areas were small in the entire tumor. The MIB-1 index was high, namely 30%, in the spindle cells, but it was low in the squamous cell carcinoma, namely less than 5%.

The squamous cell carcinoma was diagnosed to be a well or moderately differentiated type by including prominent keratinization, with slight central necrosis in the tumor. The range of hemorrhage area in the tumor was very small, and it was mostly organized. No ectopic components such as bone and cartilage, muscle, or nerves were observed in the sarcomatous element (Fig. 3). In an immunohistochemical examination, the spindle cells had the characteristics of the mesenchymal cells; they were vimentin-positive and also weakly positive for α smooth muscle actin (α -SMA). Regarding cytokeratin, it was negative for the spindle cells, and sequentially positive in the transitional portion from the spindle cells to the squamous cell carcinoma. The MIB-1 index showed a high 30% rate for the spindle cells, though it was low for the squamous cell carcinoma, with a rate of less than 5% (Fig. 3). Pleural effusion cytology was negative for the malignant cells, and no metastasis was found in the hilar lymph node or the mediastinal lymph node; and the

pathological stage was pT2N0M0 stage IB. The postoperative recovery was favorable, and the patient was released from the hospital nine days after the operation. As postoperative adjuvant therapy, four courses of 335 mg (AUC5) of carboplatin and 270 mg (175 mg/m^2) of paclitaxel were implemented, and tumor markers returned to normal levels; SCC was 0.8 ng/ml and CYFRA was 0.9 ng/ml. At six months after surgery, no recurrence has been observed.

Discussion

Pleomorphic carcinoma was first classified as a carcinoma with pleomorphic, sarcomatoid, or sarcomatous elements by the World Health Organization (WHO) in 1999,³ and in the 2003 Classification of Lung Cancers it was defined as a poorly differentiated non-small cell carcinoma, which includes squamous cell carcinoma, adenocarcinoma, and large cell carcinoma that contains

spindle cells or giant cells, and cancers that contain at least 10% spindle cells or giant cell areas.⁴⁾ Its occurrence is rare, because it accounts for only 0.3% to 1% of all lung malignant tumors.^{1,2)} In a study of constituent elements of pleomorphic carcinoma by Fishback et al. of 78 cases,¹⁾ 45% of the cases contained adenocarcinoma, 25% contained large cell carcinoma, and 8% contained squamous cell carcinoma; the remaining 22% was cancers composed of spindle cells alone, cancers composed of giant cells alone, or cancers composed of both. The number of cases that contained squamous cell carcinoma was small. In other references in the past in which 20 cases or more of pleomorphic carcinoma were studied, the number of pleomorphic carcinomas that contained squamous cell carcinoma as a constituent element was small: about 9.6% to 10%.^{5,6)} In the present case, the element of the squamous cell carcinoma occupied a broad area of 70% of the entire tumor, thus making it a rare case. As the reason that the tumor grew rapidly, we usually speculate on intratumoral bleeding after a CT-guided biopsy, or massive necrosis in the tumor. However, analyzing pathological specimen, we considered that the element of the spindle cell had enlarged rapidly, because the range of both hemorrhage area and necrotic area was small.

There are reports in which the MIB-1 index, which is an indicator of cell proliferation, of a tumor's growth speed is significantly higher in the sarcomatous element than in the carcinomatous element.⁷⁾ In the present case, too, it was less than 5% in the latter element, but it was high, namely 30%, in the sarcomatous element. Regarding the pathogenesis of the sarcomatous element, the hypothesis that the carcinoma morphologically changes into sarcoma is believed to be the most widely held opinion.⁸⁾ Therefore, in the present case, too, it is presumed that part of the squamous cell carcinoma in the present case is also presumed to have mutated into a poorly differentiated sarcomatous element with high proliferative ability, thus resulting in its rapid growth.

Regarding the prognosis, as a result of multiple classification analyses, the presence of metastasis in the lymph nodes has been reported to have a strong effect on it.¹⁾ Recent studies also suggested that both disease-free survival and overall survival with the node positive group were significantly worse than those in patients with the node negative group.^{9,10)} In studies of cases with stage I, stage II, or a higher stage of disease, the prognoses of stage I cases have been significantly favorable.^{1,5)} However, the five-year survival rate of the stage I cases was

37%, which was significantly unfavorable compared to other non-small cell lung cancers.²⁾ Especially with respect to the association with MIB-1, some reports point out that when the index is 35% or higher, the prognosis is unfavorable.⁵⁾ The present case was stage I with no metastasis in the lymph nodes, but the MIB-1 index in the sarcomatous element was a high, namely 30%, so a strict follow-up observation must be continued in this case.

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