

Pleomorphic Carcinoma: Report of a Case with Massive Pleural Effusion and Asbestos Particles

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Pleomorphic (spindle/giant cell) carcinoma (PC) is one subset of large cell carcinoma. It is well known that PC patients have a poor survival rate. This report describes a 68-year-old man with PC. The patient's tumor had a massive pleural effusion. A left lower lobectomy and partial resection of the left diaphragm, peritoneum, and parietal pleura were performed to remove the tumor. Numerous asbestos particles were found in the left lower lobe. This is the first reported case of PC which may have been caused by asbestos particles. Further investigation is needed into whether asbestos exposure causes PC. (Ann Thorac Cardiovasc Surg 2003; 9: 126–9)

Key words: pleomorphic carcinoma, asbestos, pleural effusion

Introduction

Large cell carcinoma is defined as a malignant epithelial tumor with large nuclei, prominent nucleoli, and abundant cytoplasm without the characteristic features of squamous cell, small cell, or adenocarcinoma. Fishback et al. report that pleomorphic (spindle/giant cell) carcinoma (PC) is one of the histologic subtypes of lung carcinoma.¹ PC accounts for only 0.3% of all lung malignancies. This subtype consists of large cell lung carcinomas that exhibit a spindle cell component, a giant cell component, or both, of 10% or more.² Carcinosarcoma (CS) and PC may also be different entities with similar behavior.³ The survival rate for PC patients is poor (about 10%),² and careful follow-up is needed.

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Case Report

A 68-year-old man presented to our hospital with a six-month history of shortness of breath. Smoking history was 15 cigarettes per day for 57 years. He had been a carpenter for 50 years. A chest roentgenogram at a health screening two months before admission had revealed pleural effusion (Fig. 1A). On admission, chest X-ray films showed a huge mass shadow and a massive pleural effusion (Fig. 1B). Computed tomography (CT) showed a large mass adjacent to the pleura (Fig. 2). Thoracentesis yielded 3,000 mL of bloody fluid containing irritated mesothelial cells. The biopsy specimen of the parietal pleura showed hyperplasia of the mesothelial surface cells. Irritated mesothelial cells stained negatively for carcinoembryonic antigen (CEA) and positively for colloid iron. The characteristics of the colloid iron staining did not change after treatment with hyaluronidase. The CEA level of pleural effusion was less than 1.0 ng/mL. The sialyl SSEA-1 antigen (SLX), squamous cell carcinoma-related antigen (SCC), and cytokeratin 19 fragment (CYFRA) levels were 59.2 U/mL (normal: <38 U/mL), 9.8 ng/mL (normal: <1.5 ng/mL) and 370 ng/mL (normal: <2 ng/mL), respectively. Admission laboratory data

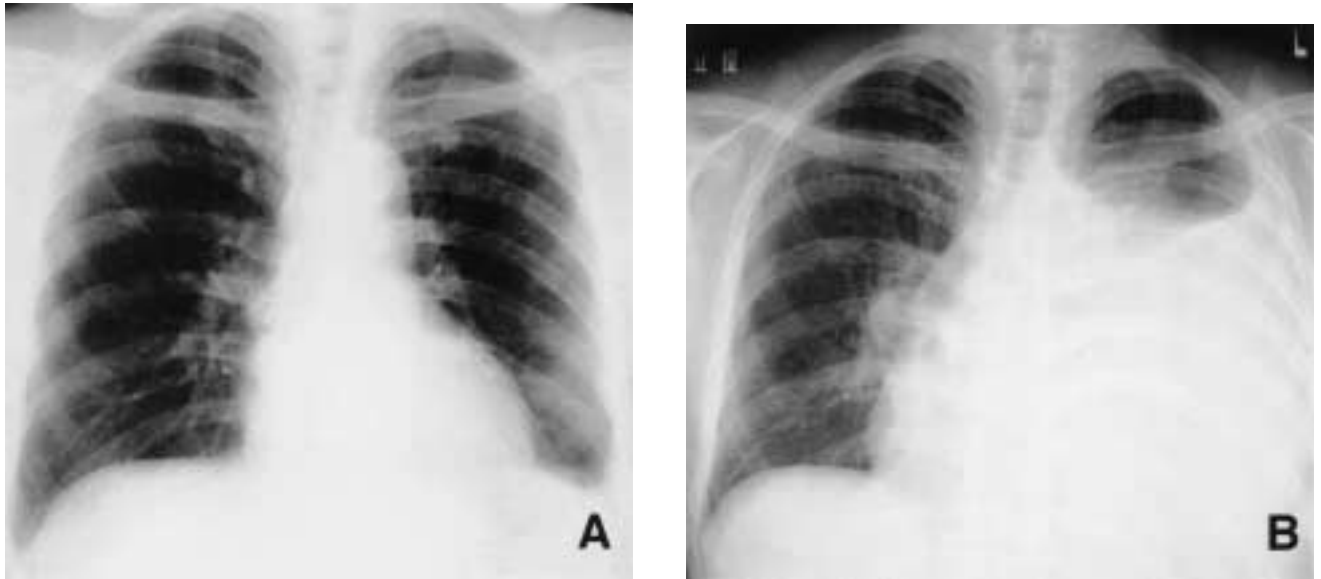


Fig. 1. A: A chest roentgenogram at a health screening two months before admission revealed pleural effusion in left lower lung field. B: On admission, a chest roentgenogram showed a huge mass shadow and massive pleural effusion.



Fig. 2. The large pleural-based mass with a massive pleural effusion in the left thorax.

included a normal blood count and bleeding profile. Arterial blood gas analysis yielded the following: pH=7.414, PO₂=87, PCO₂=39.6, and oxygen saturation of 96.8%. Spirometry revealed that forced vital capacity (FVC) was 2,450 mL (%FVC_{1.0}: 73%) and forced expiratory volume (FEV) was 1,980 mL (FEV_{1.0}: 80%). The serum CEA level was less than 1.0 ng/mL (normal: <2.5 ng/mL). Magnetic resonance imaging (MRI) revealed a dumbbell-shaped mass adjacent to the diaphragm and a collapsed lower lobe in the left thorax (Fig. 3).

Resection of the tumor and collapsed left lower lobe with partial resection of the left diaphragm, peritoneum

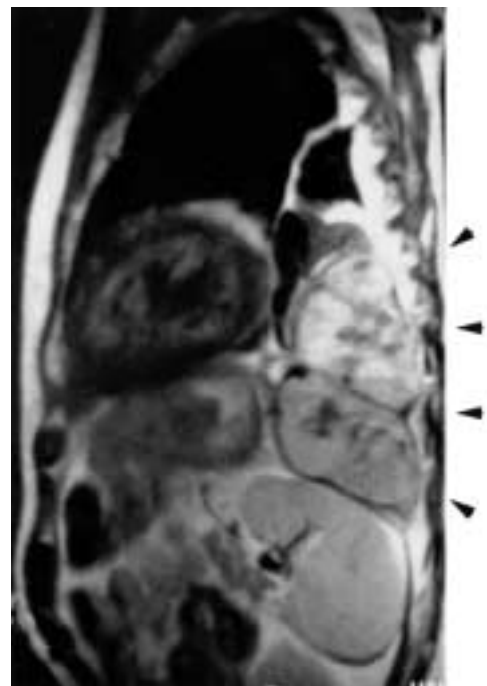


Fig. 3. A dumbbell-shaped mass adjacent to the diaphragm and a collapsed lower lobe in the left thorax (arrowheads).

and parietal pleura were performed. The patient was positioned for a right posterolateral thoracotomy. The left thorax was entered through the seventh rib bed and the eighth intercostal space with a posterolateral incision and an added vertical incision.

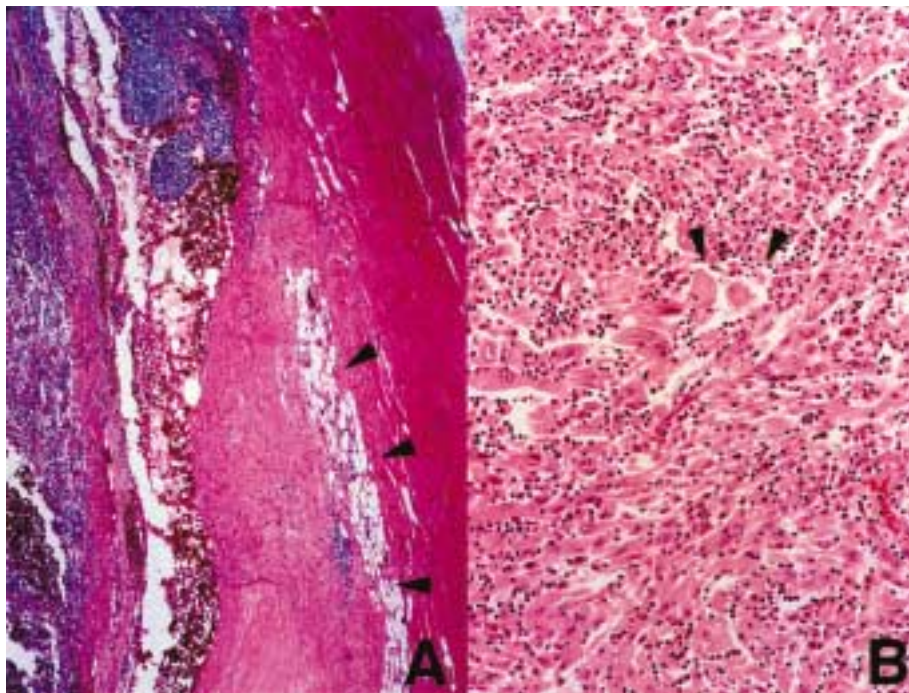


Fig. 4. A: Plaque of the parietal pleura was seen between the tumor and the diaphragm (arrowheads). B: The tumor was composed of ordinary large cell carcinoma, spindle cell carcinoma, and giant cell carcinoma. A spindle cell component simulated a sarcoma and a giant cell carcinoma showed the presence of pleomorphic and multiple nuclei (arrowheads) surrounded by inflammatory cells (hematoxylin and eosin staining).

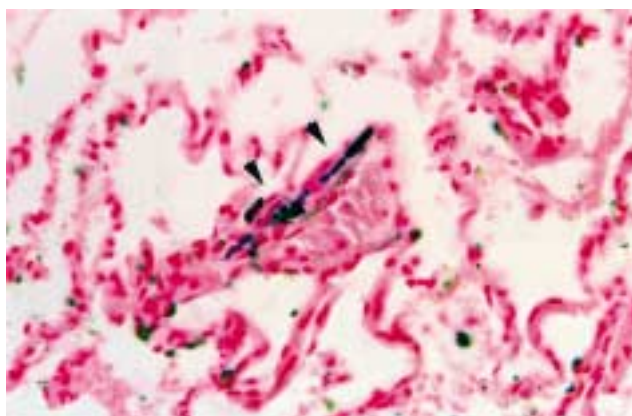


Fig. 5. Berlin blue staining showed an asbestos body (arrowheads) in the alveolar interstitium of the left lower lobe.

The excised section was reddish-gray and had a wide area covered with hemorrhage and necrosis. Microscopic examination showed many plaques of the parietal pleura (Fig. 4A). The histologic examination revealed large cell carcinoma with a spindle component and a giant cell component of 20% or more (Fig. 4B). This case was diagnosed as PC. Many asbestos particles (Fig. 5) and some metastatic lesions were seen in the resected left lower lobe. The post-thoracotomy stage was T4N0M0/stage IIIB. The patient received chemotherapy after the surgery. He has remained healthy without signs of recurrence for one year since the operation.

Discussion

Pleomorphic carcinoma (PC), one subset of large cell carcinoma, is comprised 10% or more of spindle and/or giant cell part components.²⁾ This is the first report of PC possibly caused by asbestos particles. Large cell carcinoma is defined as a malignant epithelial tumor with large nuclei, prominent nucleoli, and abundant cytoplasm without the characteristic features of squamous cell or adenocarcinoma. This tumor was stained by AE1/AE3, a monoclonal cytokeratin antibody which reacts with epithelium-derived tumors, but the tumor was not stained by HBME-1 or desmin, monoclonal antibodies which react with mesothelial and mesenchymal tumors (data not shown). Histological examination revealed a large cell carcinoma with a spindle component and a giant cell component of 20% or more. The case was diagnosed as PC.

The histologic type most common associated with PC is adenocarcinoma (45%), followed by ordinary large cell carcinoma (25%) and squamous cell carcinoma (18%).¹⁾ CS is a malignant tumor having a mixture of carcinoma and sarcoma containing differentiated mesenchymal elements. CS is also known to have similarities with PC. CS usually has a squamous or adenocarcinoma component and the histological differences between CS and PC suggest that these two types of tumors may be different entities with similar behavior.³⁾ There were foci of large cell

carcinoma without mesenchymal elements in this case.

PC usually occurs in older male smokers with large peripheral lung tumors, chest wall invasion, and metastasis.²⁾ This long term smoker also showed a large mass with pleural effusion and some metastatic lesions in the lower lobe. Asbestos fibers activate polyclonal lymphocytes and release radicals. They have an important role in the pathogenesis of immunological disorders and tumor promotion.⁴⁾ The frequency of p53 immunoreactivity in 22 patients with PC (86%) was significantly higher than that in 42 patients with squamous cell carcinoma (52%) and in 97 patients with adenocarcinoma (27%). In addition, the p53 mutations in PC were more common in exon 7, whereas those in squamous cell carcinoma and adenocarcinoma were more frequent in exon 8.⁵⁾ These findings suggest that PC needs to be distinguished from ordinary lung carcinoma and that it may be caused by promutagenic adduction. More than 30% of the tumor in this case was p53 positive (DO-1) (data not shown).

Patients with PC have a poor survival rate (about 10%),²⁾ although there was no difference in biologic behavior between PC and ordinary lung carcinoma in 37 Japanese cases.⁶⁾ Careful follow-up is needed for these patients.

Japanese workers who were exposed to asbestos are now reaching cancer age. Lung cancer deaths will continue to increase in Japan, since lung cancer is caused not only by smoking, but also in part by exposure to asbes-

tos.⁷⁾ This is the first case study of PC caused by asbestos particles. Additional studies are warranted to investigate the pathogenesis of PC from asbestos exposure.

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