Pleomorphic carcinoma of the lung: A report of six cases

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ÖZET
Akciğerin pleomorfik karsinomu: Altı olgunun sunumu


Anahtar Kelimeler: Pleomorfik karsinom, akciğer, tanı, tedavi, prognoz.

SUMMARY
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We presented six patients with pleomorphic carcinoma of the lung. There were 4 male and 2 female whose ages ranged from 43 to 64 years, with a mean age of 54.3 years. While two patients were nonsmokers, four patients were current smokers, with a mean smoking history of 52.5 (30-90) pack-years. Bronchoscopic examination detected endobronchial lesion in three patients. The diagnosis of pleomorphic carcinoma was established with cutting needle biopsy in one case and with thoracotomy in five cases. Epithelial component was squamous cell carcinoma in three cases and adenocarcinoma in the other three cases. There was bone metastasis in one case. She received chemotherapy and died two months after therapy. Among five patients who underwent surgery, pathologic staging was Stage IB in two patients, Stage IIB in two patients and Stage IV in one patient. Treatment modality was lobectomy in three cases and pneumonectomy in two cases. Survival time for patients after surgery was 2 to 20 months. In conclusion, pleomorphic carcinoma is a rare tumor of the lung. Diagnosis is frequently established with thoracotomy. These tumors have poor prognosis.

Key Words: Pleomorphic carcinoma, pulmonary, diagnosis, treatment, prognosis.

Pleomorphic carcinoma was recently classified as a subgroup of the general category of carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements. Histologically, a pleomorphic carcinoma is defined as either a non-small cell lung carcinoma combined with neoplastic spindle and/or giant cells or a carcinoma that consists of only spindle and giant cells. Pleomorphic component should comprise at least 10% of the neoplasm (1). Pleomorphic carcinoma, quoted by Chang and associates, is primarily found in the oral cavity, larynx, breast, kidney, urinary bladder, uterus, and conjunctiva (2). It is considered to be a rare tumor of the lung, which accounts for only 0.3% of all lung malignancies (3). The rarity of pleomorphic carcinomas and their histologic similarity to other neoplasms, result in difficult diagnosis (2). It was reported that these tumors invade mediastinal structures, pleura, and chest wall, and show signs of early distant metastases (2,4,5). Its prognosis is poor, with a median survival time of only 10 months (3). We presented six patients with pleomorphic carcinoma of the lung.

MATERIALS and METHODS
Between 2001 and 2005, we retrospectively reviewed the records of pathology department. We identified six patients with pleomorphic carcinoma of the lung during that period. Pathologic preparations of all patients were reexamined by the same pathologist. Hematoxylin and eosin-stained sections were present in all cases. Immunohistochemical staining for keratin, epithelial membrane antigen (EMA) and vimentin was performed in three cases. The diagnosis of pulmonary pleomorphic carcinoma was based on the criteria set by the World Health Organization (6). The medical records of the patients were analyzed retrospectively. Records were reviewed for the following: age, sex, symptoms, history of smoking, radiological features, diagnostic methods, pathologic findings, stage of the tumor, and treatment. Follow-up information for patients was obtained from direct patient or family contact on January 2006.

RESULTS
The present study included six patients. Four patients were male and two patients were female. Their ages ranged from 43 to 64 years, with a mean age of 54.3 years. While two patients were nonsmoker, four patients were current smoker, with a mean smoking history of 52.5 (30-90) pack-years. The most frequent symptom was chest pain. This data was shown in Table 1.

Chest X-ray demonstrated mass lesion in all patients. Mass was located on the right middle zone in two cases, on left lower zone in one case, on left upper and middle zone in one case, on right upper zone in one case, and on left upper zone in one case. Table 2 summarizes computed tomography (CT) and bronchoscopy findings. Tumor was located in upper lobes in four cases and in lower lobes in two cases. On bronchoscopic examination, the tumor was located peripherally in four cases and centrally in two cases. Pathologic diagnosis of bronchoscopic biopsies was nonsmall cell carcinoma in one case and squamous cell carcinoma in one case. Bronchoscopic biopsies were not diagnostic in remaining 4 cases.
The pathologic diagnosis of pleomorphic carcinoma was made with cutting needle biopsy in one case (case 4). Pathologic diagnosis was made at thoracotomy in five patients. Immunohistochemical staining was performed in three cases. Epithelial cells were stained with keratin and EMA, but not with vimentin. Spindle cells were stained with vimentin, but not with keratin and EMA. Epithelial component was squamous cell carcinoma in three cases and adenocarcinoma in the other three cases (Figure 1). There was bone metastasis in one case. She received chemotherapy and died two months after therapy. Treatment modality was lobectomy in three cases and pneumonectomy in two cases. Among five patients who underwent surgery, pathologic staging was Stage IB in two patients, Stage IIB in two patients and Stage IV in one patient. Survival time for four patients after diagnosis was between 2 and 20 months. Clinical data including diagnosis, pathology, stage and treatment on six patients of pleomorphic carcinoma were represented in Table 3.

### Table 1. Clinical data in six patients with pleomorphic carcinoma.

<table>
<thead>
<tr>
<th>No</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Smoking status</th>
<th>History of smoking (pack-years)</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>Smoker</td>
<td>90</td>
<td>Chest pain, weight loss</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>M</td>
<td>Smoker</td>
<td>30</td>
<td>Chest pain, cough, sputum, weight loss</td>
</tr>
<tr>
<td>3</td>
<td>51</td>
<td>M</td>
<td>Smoker</td>
<td>40</td>
<td>Chest pain</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>F</td>
<td>Non-smoker</td>
<td>-</td>
<td>Chest pain</td>
</tr>
<tr>
<td>5</td>
<td>63</td>
<td>M</td>
<td>Smoker</td>
<td>50</td>
<td>Chest pain, haemoptysis</td>
</tr>
<tr>
<td>6</td>
<td>43</td>
<td>F</td>
<td>Non-smoker</td>
<td>-</td>
<td>Haemoptysis</td>
</tr>
</tbody>
</table>

### Table 2. CT and bronchoscopy findings.

<table>
<thead>
<tr>
<th>No</th>
<th>Involved lobe</th>
<th>CT findings</th>
<th>Bronchoscopy findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Finding</td>
<td>Location</td>
</tr>
<tr>
<td>1</td>
<td>Right upper</td>
<td>Atelectasis</td>
<td>Right upper</td>
</tr>
<tr>
<td>2</td>
<td>Posterior segment of right upper</td>
<td>Mass</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Left lower</td>
<td>Nodule</td>
<td>Left lower</td>
</tr>
<tr>
<td>4</td>
<td>Left upper</td>
<td>Mass</td>
<td>Apicoposterior segment of left upper</td>
</tr>
<tr>
<td>5</td>
<td>Left upper</td>
<td>Mass</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>Superior segment of right lower</td>
<td>Mass</td>
<td>-</td>
</tr>
</tbody>
</table>

DISCUSSION

Pleomorphic carcinoma is an infrequent tumor of the lung (2,3). It is defined as "a poorly differentiated non-small cell lung carcinoma, namely squamous cell carcinoma, adenocarcinoma or large cell carcinoma, containing spindle cells and/or giant cells, or a carcinoma consisting
only of spindle and giant cells”. Pleomorphic component should comprise at least 10% of the neoplasm (1). According to this definition, we detected only six cases of pulmonary pleomorphic carcinoma during five years. More than 1000 cases with primary lung cancer were diagnosed annually in our center. These results pointed out that this tumor was a rare tumor of the lung.

Pleomorphic carcinomas occur mainly in men who smoke heavily (5,7-9). The male-female ratio was 3.1:1 and 9:1 in two previous reports (5,7). In a previous study of 75 cases of pulmonary carcinoma with pleomorphic, sarcomatoid, or sarcomatous elements, 92% of the patients were smoker (8). The patients’ age ranged from 31 to 84 years, with a mean age of 57 years (7). In our series, the male-female ratio was 2:1 and 67% of the patients were smoker. The mean age of our patients was 54.3 years. Chang et al. reported that all patients were symptomatic (2). The most frequent symptoms were cough, haemoptysis, chest pain and weight loss in previous reports (2,5,7). Chest pain was the most frequent symptom in the present study. Pleomorphic carcinoma frequently presents as peripheral lesion. It also showed a predilection for the upper lobes (5,7).

Similarly, tumor showed peripheral localization and a predilection for upper lobes in our series. The diagnosis of pleomorphic carcinoma was frequently made with thoracotomy (5,10). Kim et al. reported that percutaneous needle biopsy revealed the diagnosis of pleomorphic carcinoma in none of their patients (5). In our series, the diagnosis was made with thoracotomy in five cases and with cutting needle biopsy in one case. Bronchoscopic examination detected endobronchial mass lesion in three cases. Although bronchoscopic biopsies revealed a diagnosis of lung cancer in two cases it was insufficient to diagnose a tumor of the lung as pleomorphic carcinoma. According to our opinion, the diagnosis of mixed tumors such as pleomorphic carcinoma with bronchoscopy is difficult because bronchoscopic biopsies can yield small amount of tissue for pathological examination. Epithelial component was squamous cell carcinoma in three cases and adenocarcinoma in the other three cases in the present study. Chang et al. determined that epithelial component was adenocarcinoma in nine patients, squamous cell car-
cinoma in four cases and undifferentiated carcinoma in three cases (2). According to Kim et al., the most frequent epithelial component was large cell carcinoma, followed by squamous cell carcinoma (7). Immunohistochemical staining may play a role in establishing the diagnosis of pleomorphic cell carcinoma of the lung in instances where carcinomatous differentiation is poor at the light microscopic level (2,10). Several antibodies are used to differentiate components of pleomorphic carcinoma (2,8-12). Vimentin and cytokeratin are the most common used antibodies for immunohistochemical staining. While epithelial cells were stained with keratin, spindle cells were stained with vimentin (2,8,10). Immunohistochemical studies including vimentin and keratin were performed in our three cases. The carcinomatous component was positive for keratin and negative for vimentin and the spindle cell component was positive for vimentin and negative for keratin in these cases.

Many reports pointed that these tumors invade mediastinal structures, pleura and chest wall, and show signs of early distant metastases (2,4,5,7). It was reported that 15 of 30 patients had T3 and/or N1-N2 disease (7). Chang et al. studied 16 cases of pulmonary pleomorphic carcinoma (2). Their series included nine inoperable and seven operable cases. Among seven patients who underwent surgical resection, four of them had mediastial, pleural and chest wall invasions and three of them had regional lymph node metastases. Our two patients had Stage IV disease. There were two patients with N1 disease. None of our patients had N2 disease. We estimated survival for five patients. In our study, survival time was two months in two patients, eight months in one patient, 10 months in one patient and 20 months in one patient. It is accepted that these tumors have poor prognosis (2,5). It was reported that 6 of 10 patients died within 5 months after surgery (5). Chang et al. found that the median survival was 3 months (2). A previous report determined a median survival time of 10 months (3). Raveglia et al. reported that 16 of 20 patients with pleomorphic carcinoma died from early distant metastases (13). In their series, the median duration of disease-free survival was 5 months and the median duration of overall survival was 8 months. In conclusion, pleomorphic carcinoma is a rare tumor of the lung. Diagnosis is frequently established with thoracotomy. These tumors have poor prognosis.

REFERENCES