Radiologically Occult Lung Cancer in the Peripheral Region

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A rare case of radiologically occult lung cancer in the peripheral region beyond bronchoscopic visibility is reported. A 69-year-old female was referred because of positive sputum cytology. Despite detailed bronchoscopic and otorhinoralyngologic examinations, the source of malignant cells was not localized. During the follow-up period, squamous cell carcinoma of the lung periphery was detected radiologically three years after its presence was detected in sputum. Awareness of the existence of this type of cancer and careful follow-up are important in the management of patients with positive sputum cytology and no evidence of cancer.

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Key words: sputum cytology, bronchoscopy, squamous cell carcinoma

Introduction

Sputum cytology is useful for the early detection of squamous cell carcinoma of the central airway. However, despite the presence of malignant cells in sputum, the source occasionally cannot be determined. It is quite important to be aware of potential causes and avoid overlooking anything. We report a case of peripherally located occult lung cancer that was detected radiologically three years after the detection of the positive sputum cytology.

Case Report

In October 1985, a 69-year-old homemaker with angina pectoris was referred to our hospital because squamous metaplastic cells with marked atypia were detected in sputum. She had smoked 20 cigarettes per day for 54 years, and complained of a small amount of sputum. Physical and laboratory examinations including tumor markers were unremarkable. Chest X-rays, computed tomography, and otorhinolaryngologic examinations were normal. Bronchoscopic examination revealed sputum on the left upper bronchus, but brushing cytology was negative. We could not perform systematic brushing of all subsegments because of accompanying heart disease.

In April 1986, sputum cytology showed squamous cell carcinoma. However, chest X-rays, bronchoscopy, and otorhinolaryngologic examinations did not localize the source. In October 1987, she showed squamous metaplastic cells with moderate atypia in sputum and a normal chest X-ray.

In September 1988, a nodule appeared at the upper subdivision of the left anterior segment on chest X-ray (Fig. 1) and computed tomography (Fig. 2), and malignant cells presented in sputum again. We failed to establish the diagnosis bronchoscopically, and she underwent exploratory thoracotomy for diagnosis. A white nodule measuring 15×11 mm was located at

Fig. 1. Chest X-ray showing a well-defined nodule 15 mm in diameter in the left upper field (arrow).
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Fig. 2. Chest computed tomography showing a lobulated nodule with pleural retractions in the upper subsegment of the left anterior segment.

Fig. 3. Pathological specimen showing squamous cell carcinoma. The lobulated tumor was located in the distal portion of the medial branch of the left upper subsegmental bronchus (HE stain, ×4).

Discussion

Malignant cells in sputum originate from tumors in the upper aerodigestive tract or the tracheobronchial tree. One study of screening in the United States revealed 22 lung cancer (79%) and four upper aerodigestive cancer patients (14%) among 28 patients with positive sputum cytology and a normal chest radiograph (1). In the remaining two patients (7%), however, cancer could not be found. Another study in Japan also showed that repeated bronchoscopic examinations detected only 33 lung cancers (77%) in 43 patients with positive sputum cytology (2). Not all the sources of malignant cells are determined by detailed examinations.

The range of bronchoscopic visibility is within fifth order bronchi. Squamous cell carcinoma of the lung mainly develops from the central airway within its visibility: the most incident location is in the segmental bronchi, and the second is in the subsegmental bronchi (3). However, 15% of all squamous cell carcinoma originates in the periphery beyond bronchoscopic visibility (4). Peripheral squamous cell carcinoma, like the central type, arises from the bronchial or bronchiolar mucosa (4).

Only five cases of occult squamous cell carcinoma in the fifth bronchi or more distal have been previously described in detail (5–7) (Table 1). In three cases, the location of the cancer was identified by systematic brushing cytology under frequent bronchoscopic examinations (5). In one case, thin-section computed tomograph showed local thickening of the peripheral bronchial wall and assisted the localization (6). In the remaining case, lung cancer finally appeared as a nodule measuring 20×15 mm on X-ray three years after the presence was detected in sputum (7). Although radiologically occult peripheral lung cancer is rare, it does exist and its localization is difficult.

Computed tomography, especially thin-section computed tomography, may provide useful information regarding the location of cancer. Even with the optimal technique of plain radiography and careful interpretation of films, early detection of peripheral lung cancer is difficult (9). Computed tomography has a high sensitivity to detect a nodule as small as 5 mm (10). In addition, thin-section computed tomography can detect endobronchial lesions by revealing a thickening of the bronchial wall or occlusion of the bronchial lumen (6). Computed tomography is more valuable than plain radiography to detect small lung cancer in the peripheral region.

Determining the appropriate length of follow-up in patients with positive sputum cytology but no evidence of cancer is a practical problem. The average duration from detection of cancer cells in sputum to radiographic diagnosis can be as long as 3.26 years (11). However, the duration from 10 mm, which is the minimum detectable size by plain radiography, to 30 mm in diameter is estimated to be only one year (12). Squamous cell carcinoma grows rapidly after reaching the radiologically detectable size. Follow-up examinations, therefore, should be performed annually for at least four years to detect the lesion before the disease advances.

Repeat examinations over a long period can harm patients physically and mentally. It is important that patients understand the information of their own disease and the proposed procedures, although revealing the truth to cancer patients is a difficult problem in Japan (13). At present in Japan, 86% of the patients with early cancer and 71% of those with advanced cancer wish to know their true diagnosis (13). Physicians,
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Table 1. Reported Cases of Radiologically Occult Squamous Cell Carcinoma in the Peripheral Region

<table>
<thead>
<tr>
<th>Age/ Gender</th>
<th>Smoking Index*</th>
<th>Cancer Site*</th>
<th>Size</th>
<th>Times of Bronchoscopy</th>
<th>Method of detection</th>
<th>Author (Reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>76/M</td>
<td>840</td>
<td>rS³b</td>
<td>6mm</td>
<td>9</td>
<td>Frequent bronchoscopic brushings</td>
<td>Sato (5)</td>
</tr>
<tr>
<td>67/M</td>
<td>1750</td>
<td>rS³b</td>
<td>6mm</td>
<td>7</td>
<td>Frequent bronchoscopic brushings</td>
<td>Sato (5)</td>
</tr>
<tr>
<td>78/M</td>
<td>1000</td>
<td>rS³</td>
<td>8mm</td>
<td>9</td>
<td>Frequent bronchoscopic brushings</td>
<td>Sato (5)</td>
</tr>
<tr>
<td>64/M</td>
<td>Unknown</td>
<td>rS³</td>
<td>3mm</td>
<td>3</td>
<td>Thin-section CT and bronchoscopic brushings</td>
<td>Foster (6)</td>
</tr>
<tr>
<td>65/M</td>
<td>Unknown</td>
<td>IS³</td>
<td>20mm</td>
<td>3</td>
<td>Follow-up radiographs (3 years later)</td>
<td>Bai (7)</td>
</tr>
<tr>
<td>69/F</td>
<td>1080</td>
<td>IS³c</td>
<td>15mm</td>
<td>3</td>
<td>Follow-up radiographs (3 years later)</td>
<td>Present case</td>
</tr>
</tbody>
</table>

M: male, F: female, CT: computed tomography. *Smoking index is calculated as (number of cigarettes per day) × (years of smoking). †According to the nomenclature system of the Japan Lung Cancer Society (8).

therefore, should explain the information of the disease to cancer patients in as much detail as possible.

In conclusion, although radiologically occult peripheral lung cancer is rare, awareness of its existence and careful follow-up are important in the management of patients with positive sputum cytology but no evidence of cancer.

References