Image Characteristics of ALK-positive non-small cell lung cancer

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Purpose

<Background>
The fusion between echinoderm microtubule-associated protein-like 4 (EML4) and anaplastic lymphoma kinase (ALK) has been identified in a subset of non-small cell lung cancers (NSCLCs). EML4-ALK is most often detected in never or light smokers, which accounts for 4-7% of NSCLCs, and has unique pathologic features. Patients were prone to be younger at diagnosis. In histological examinations, tumors have been diagnosed with adenocarcinoma, and signet-ring cells and mucinous cribriform pattern and solid carcinomas with mucus formation are frequently seen.

Recently ALK inhibitor has become an effective treatment for patients with ALK-positive NSCLCs. Several image characteristics of EGFR mutation-positive NSCLC has been reported, but there is no report about image characteristics of ALK-positive NSCLC. If there are specific image features about ALK-positive NSCLC, they might be useful in diagnosing ALK-mutated NSCLC.

<Purpose>
The purpose of this study is to clarify the image characteristics with ALK-positive NSCLCs.
Methods and Materials

<Subjects and Methods>

Patient selection

Between March 2003 and November 2011, 19 patients with ALK-positive NSCLS at our hospital were analyzed. We retrospectively reviewed patient characteristics and image findings of chest X-ray and Computed tomography scans (CT).

Radiologic methods

The whole-body CT examinations were used multidetector-low CT (MDCT) machine, with iodinated contrast material from lower neck to pelvic floor at the end of suspended inspiration. CT images were obtained with a scan delay of 90 sec, and reconstructed to 5mm slice thickness. Thin section chest CT with 1 mm reconstruction thickness was also performed for evaluating primary tumor.
Results

Nineteen patients with ALK-positive NSCLCs were enrolled in this study. There were 6 males and 13 females, and the median age was 54 years (range, 20-72 years), including 13 non-smokers and 6 smokers. All cases were adenocarcinoma except one adenosquamous carcinoma (Table. 1). In 11 cases, primary lesions showed solid mass with peripheral ground-glass opacities, including 4 cases with lymphangitis carcinomatosa (Table. 2, Figure. 1, 2, 3). In 10 cases of 12 with N2/3 diseases, metastatic lymph nodes were serial combined swelling, and 6 cases demonstrated dirty fatty change surrounding ring enhancement (Figure. 4). Initial CT scan, 10 patients showed pulmonary metastases, of these 7 cases showing part-solid nodules that were considered peripheral local lymphangitis (Figure. 5).

There were no specific features regarding liver, bone and brain metastases.

Discussion

Primary lesions of NSCLC can be divided into 3 types based on their CT characteristics; 1) Ground-glass opacity (GGO), 2) focal GGO with solid central components, 3) solid nodules. 58% of our cases, primary lesion showed solid mass with peripheral GGO, and 70% of pulmonary metastases were accompanied by GGO. ALK-positive NSCLC might have a tendency to involve lung field lesions by GGO. Pathological features of ALK-positive NSCLC has been reported that extracellular mucus was noted in 69% cases, and alveolar spaces were often expanded by mucus at the tumor periphery, and solid or acinar growth pattern, cribriform structure, presence of mucus cells (signet-ring cells or goblet cells), abundant extracellular mucus, lack of lepidic growth, and lack of significant nuclear pleomorphism were more common in ALK-positive cancers. In another report, which is stated that ALK-positive lung adenocarcinoma showed significant associations with intra- and/or extra-cytoplasmic mucin, and cribriform pattern with excessive extracytoplasmic mucin. In our cases of primary lesion surrounded by GGO, biopsy slides were available for 5 cases, they are all poorly differentiated, and were associated with mucus production. It is conceivable that extracellular mucus appears to be GGO around the tumor in CT images.

In NSCLC, characteristic in the form of lymph node metastases has not been reported almost. Initial CT scan, 83% of our cases with N2 or N3 diseases, metastatic lymph nodes were combined and swelled, surrounded them dirty fatty change, so had been a series of masses. Pathologically, it is stated that a solid signet-ring cell pattern and a mucinous cribriform pattern were present at least focally in the 78% of ALK-positive tumors, but were 1% in ALK negative tumors. In lung carcinoma with signet-ring cell, lymph vessel invasion and lymph node metastasis were significantly more frequent. Therefore, image findings
of ALK-positive NSCLCs were prone to show local and extranodal lymphatic extents, and they seemed to have expanded lymph ducts, and hilar or mediastinal lymph nodes tended to coalesce and spread out. Furthermore, it is conceivable that GGO around the tumors were considered mucus as well as peripheral local lymphangitis.
### Table 1: Patients characteristics

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<table>
<thead>
<tr>
<th>Results</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT appearance of Primary tumor</td>
<td></td>
</tr>
<tr>
<td>Solid</td>
<td>8</td>
</tr>
<tr>
<td>Part solid</td>
<td>11</td>
</tr>
<tr>
<td>GGO</td>
<td>0</td>
</tr>
<tr>
<td>Metastatic sites (initial CT scan)</td>
<td></td>
</tr>
<tr>
<td>Intrapulmonary</td>
<td>10</td>
</tr>
<tr>
<td>Brain</td>
<td>6</td>
</tr>
<tr>
<td>Bone</td>
<td>6</td>
</tr>
<tr>
<td>Pleura</td>
<td>3</td>
</tr>
<tr>
<td>Liver</td>
<td>2</td>
</tr>
<tr>
<td>Pericardium</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid grand</td>
<td>2</td>
</tr>
<tr>
<td>Lymphangitis carcinomatosa</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table 2:** CT Findings of ALK-positive NSCLCs

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![CT scans](image1.png)

**Fig. 1:** Primary lesions: part 1

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Fig. 2: Primary lesion: part 2

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Fig. 3: Lymphangitis carcinomatosa

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Fig. 4: Metastatic lymph nodes

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Fig. 5: Intrapulmonary metastases

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Conclusion

ALK-positive NSCLCs were prone to show lung parenchymal lesions surrounded by GGO or with ground grass halo. In N2 or N3 diseases, metastatic lymph nodes tended to be combined and swelled, series of mass were formed and surrounded by dirty fatty change. In addition, the initial CT scan, intrapulmonary metastases were more frequent confirmed.

These CT imaging characteristics may be associated with ALK-positive NSCLC, and useful to be determined the appropriate strategy for patients with ALK gene positive or not.
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