Comparison of High-resolution CT Findings between Miliary Metastases and Miliary Tuberculosis

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Purpose: To compare the findings of high-resolution computed tomography (HRCT) between patients with miliary metastases and miliary tuberculosis.

Materials and Methods: Between May 1998 and April 2002, 11 patients with miliary metastases and 18 with miliary tuberculosis underwent HRCT, and we reviewed the findings. In miliary metastases, the primary lesions were adenocarcinoma of the lung \((n=2)\), stomach \((n=1)\), or pancreas \((n=1)\), or of unknown origin \((n=5)\), and papillary carcinoma of the thyroid \((n=2)\). Two radiologists blinded to the clinical and pathologic data reached a consensus regarding nodule size and margin, their distribution and coalescence, interstitial involvement, and other ancillary HRCT findings. Data were analyzed using the chi-square test.

Results: CT scans showed numerous 1 to 5-mm nodules randomly distributed throughout both lungs of all patients. Nodules larger than 1.5 mm in diameter were more often seen in miliary metastases \((81.9\%)\). In six \((54.5\%)\) patients with miliary metastases and in three \((16.7\%)\) with miliary tuberculosis, nodule size varied \((p<0.05)\).

Pleural effusion occurred in three \((27.3\%)\) patients with miliary metastases and three \((16.7\%)\) with miliary tuberculosis. Interlobular septal thickening \((100\%)\) and peribronchovascular thickening \((63.6\%)\) were more common in miliary metastases than in miliary tuberculosis \((p<0.01)\). Lymph node enlargement was seen in 11 \((100\%)\) patients with miliary metastases and five \((27.8\%)\) with miliary tuberculosis \((p<0.001)\).

Conclusion: At HRCT, lymph node enlargement and both interlobular and peribronchovascular thickening are more commonly observed in miliary metastases than in miliary tuberculosis.

Index words: Lung neoplasms, CT
Lung neoplasms, metastases
Tuberculosis, pulmonary
Miliary lung disease is characterized by the development of numerous small millet seed nodular lesions throughout the lungs, a pattern which indicates hematogenous or lymphatic spread. In such cases, accurate localization of pathologic change occurring within the lobule could be helpful in the differential diagnosis of certain pulmonary parenchymal diseases investigated by means of HRCT (1, 2). Nodules distributed both along the course of visible arteries and along lobular borders (septal, pleural, or fissural surfaces) have been classified as "panlobular" or "random" (hematogenous) (3). Random distribution of miliary nodules occurs during the hematogenous spread of tuberculosis, fungal infection, or metastases from a variety of primary sources (2, 4), the most common causes of these nodules are miliary tuberculosis and metastases. In some patients, miliary metastases resembling miliary tuberculosis occur in the absence of a known primary tumor and differentiation between miliary tuberculosis and metastases at HRCT, of great importance for treatment, is troublesome. To our knowledge, prior studies have simply stated that differentiated protein derivative; and (c) a good response to antituberculous chemotherapy.

HRCT scanning was performed in the absence of intravenous contrast material, using a Highlight (General Electric Medical Systems, Milwaukee, Wis., U.S.A.) or Somatom-Plus scanner (Siemens Medical Systems, Erlangen, Germany). Scans of 1 mm thickness were obtained at 10-mm intervals, from the lung apices to the bases, using a 35-cm field of view, a 512×512 reconstruction matrix, 137 kV, 220–270 mA, and 1-second scanning time. Images were reconstructed using a high spacial frequency algorithm. For lung windows, level/width was -600 HU/1,500 HU, and for mediastinal windows the corresponding setting was 0/300 HU.

Two radiologists analyzed all the images, and final decisions regarding the findings were determined by consensus. The assessment criteria used were as follows: size, margin, distribution and coalescence of nodules; ground-glass opacity, and interlobular septal and peribronchovascular thickening. Nodules were classified as < 1.5, 1.5–3 or > 3.0 mm in diameter; where their size was not uniform, a consensus was reached. Margins were classified as well or poorly defined: well defined if the nodule was sharply and distinctly separated from surrounding normal lung; or poorly defined if it was hazy or indistinct, with its edge merging imperceptibly into surrounding lung. Distribution was classified as predominantly in the upper, middle, or lower zone of the lung, and as mainly central or peripheral. A location superior to the aortic arch was deemed ‘upper zone’; one inferior to the inferior pulmonary vein was ‘lower zone’; and a location between the aortic arch and the inferior pulmonary vein was ‘middle zone’. Lung cortex was defined as one or two rows of well-organized and well-defined secondary pulmonary lobules, which together formed a layer about 3–4 cm in thickness. An area of slightly increased attenuation in which the bronchial walls and vessels remained visible was considered as ground-glass opacity, and apparent thickening of the bronchial wall and an apparent increase in size or change in the nodular appearance of the pulmonary arteries was identified as peribronchovascular interstitial thickening. In addition the presence of pleural effusion or a lymph node was recorded. A lymph node was considered enlarged when the short-axis di-
ameter was more than 1 cm at the hilum and mediastinum.

To determine whether differences in HRCT findings between the miliary metastasis and miliary tuberculosis groups were statistically significant, the Chi-square test was used. Differences in the frequency of each abnormality in each subgroup were evaluated using Fisher’s exact test when the former test was inappropriate. Probability values of less than 0.05 were considered significant. For statistical analysis, a software package (SAS for windows, version 6.12) was used.

Results

CT scans depicted numerous tiny 1 to 5-mm nodules distributed throughout both lungs. Nodules of more than 1.5 mm in diameter were seen in 81.9% (9/11) patients with miliary metastases and in 50.0% (9/18) with miliary tuberculosis. There was no significant difference in the size of nodules between the two groups (Table 1).

Table 1. Comparison of Size of Nodules

<table>
<thead>
<tr>
<th></th>
<th>&lt; 1.5 mm</th>
<th>1.5-3 mm</th>
<th>&gt; 3 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miliary metastases [n = 11]</td>
<td>2 (18.2%)</td>
<td>6 (54.5%)</td>
<td>3 (27.3%)</td>
</tr>
<tr>
<td>Miliary tuberculosis [n = 18]</td>
<td>9 (50.0%)</td>
<td>7 (38.9%)</td>
<td>2 (11.1%)</td>
</tr>
</tbody>
</table>

Nodules varied in size in 54.5% (6/11) patients with miliary metastases and in 16.7% (3/18) of those with miliary tuberculosis ($p < 0.05$). In 72.7% (8/11) of patients with metastases and 72.2% (13/18) of tuberculosis patients, a well-defined margin was observed. Lower zone predominance was seen in 54.5% (6/11) with metastases and in 16.7% (3/18) of tuberculosis patients. In the miliary metastasis group, interlobular septal thickening (100%; 11/11) and peribronchovascular thickening (63.6%; 7/11) were more common than in the miliary tuberculosis group ($p < 0.01$). Lymph node enlargement was visible in 100% (11/11) patients with miliary metastases and 27.8% (5/18) with miliary tuberculosis. Lymph node enlargement was more common in the miliary metastasis group ($p < 0.001$); the right lower paratracheal area was

![A](image1)  
**Fig. 1.** A 61-year-old man with miliary metastases and unknown primary adenocarcinoma.  
A. CT scan obtained at the level of the bronchus intermedius shows nodules in random distribution in the lungs. Also note that peribronchovascular thickening (arrow).  
B. CT scan obtained at the level of the inferior pulmonary vein shows interlobular septal thickening (arrow) are seen in the right lung.  
C. Transverse thin-section CT scan obtained at the level of the top of the aortic arch shows a lymph node enlargement (^) in right lower paratracheal area.
the most common site, identified in 64% of patients (Table 2).

Discussion

It has been shown at HRCT that in patients with miliary metastases (9, 10) or tuberculosis (6), the micronodules in the secondary pulmonary lobule were randomly distributed. In most miliary metastases (81.8%), the diameter of the nodule was more than 1.5 mm. The nodules involved in miliary metastases were larger than those in miliary tuberculosis (6). In addition, variations in size were more frequently observed in patients with miliary metastases \( p < 0.05 \). These HRCT appearances were in agreement with those of Lee et al. (5) and Oh et al. (6). A well-defined nodular margin was not, however, helpful for differential diagnosis between miliary metastasis and tuberculosis. In terms of distribution patterns, there was no statistically significant difference between miliary metastases and tuberculosis.

Our study showed that most patients with miliary metastases had abnormalities of the interlobular septa and peribronchovascular bundles, and this may indicate lymphangitic spread of the tumor. Lung lesions were mainly multiple well-defined nodules, and lymphangitic spread was observed in some areas surrounding the nodules. It therefore seemed reasonable to assume that hematogenous metastatic nodules could cause local lymphangitic spread of the tumor along pulmonary vessels in contact with the nodule. At HRCT, this spread appeared as thickening of bronchovascular bundles or perilobular structures connected to the nodule. It was believed that malignant cells were carried hematogenously and dispersed into the interstitium. Thereafter, they entered the lymphatics, giving rise to lymphatic spread. To explain the radiologic abnormalities seen in bronchovascular bundles and interlobular septa, four mechanisms have been proposed \( 11-13 \): (a) obstruc-

Table 2. Comparison of Miliary Metastases and Tuberculosis

<table>
<thead>
<tr>
<th></th>
<th>Nodules</th>
<th>Interstitial involvement</th>
<th>Ground glass opacity</th>
<th>Pleural effusion</th>
<th>Lymph node enlargement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Size (&gt;1.5 mm)</td>
<td>Diversity in size</td>
<td>Size</td>
<td>Well defined margin</td>
<td>Distribution</td>
</tr>
<tr>
<td>Metastases ( (n = 11) )</td>
<td>9 (81.9%)</td>
<td>6 (54.5%)</td>
<td>6 (54.5%)</td>
<td>4 (36.4%)</td>
<td>10 (90.9%)</td>
</tr>
<tr>
<td>Tuberculosis ( (n = 18) )</td>
<td>9 (50.0%)</td>
<td>3 (17%)</td>
<td>13 (72.2%)</td>
<td>3 (16.7%)</td>
<td>13 (72.2%)</td>
</tr>
<tr>
<td>( p )-value</td>
<td>( p &gt; 0.05 )</td>
<td>( p &lt; 0.05 )</td>
<td>( p &gt; 0.05 )</td>
<td>( p &gt; 0.05 )</td>
<td>( p &gt; 0.05 )</td>
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LZP; lower zone predominance, ILST; interlobular septal thickening, PVBT; peribronchovascular thickening

Fig. 2. A 37-year-old man with miliary tuberculosis.

**A.** Transverse thin-section CT scan obtained at the level of the lung apex shows miliary nodules in both lungs and areas of airspace consolidation in left lung.

**B.** Transverse thin-section CT scan obtained at the level of the inferior pulmonary vein shows typical tiny numerous miliary nodules in both lungs. Note that coalescence of nodules are seen at lateral basal area.
tion by malignant cells within lymphatics may cause their distension; (b) growth of a tumor within the interstitium may be a direct cause of interstitial thickening; (c) interstitial pulmonary edema may be related to lymphatic involvement; and (d) desmoplastic reaction may be related to malignant spread. According to Hirakata et al. [14], lymphangitic spread was histopathologically confirmed in 11 (79%) of 14 pulmonary metastatic patients. However, the pulmonary arteries leading to the metastatic nodules were often thrombosed by the tumor, and a tumor thrombus might also cause the thickened bronchovascular bundle seen at HRCT [12]. Similarly, miliary infection, particularly tuberculosis, can cause interstitial abnormalities, typically septal lines [6]. McGuinness et al. [15] assumed that innumerable tiny granulomas scattered throughout the pulmonary interstitium could account for diffuse intra- and interlobular thickening. In this study, interlobular septal thickening was present in 9 of 18 patients with tuberculosis. Bronchovascular bundle thickening and interlobular septal thickening were considered to be characteristic points of differentiation between miliary metastases and miliary tuberculosis.

The ancillary findings of miliary metastases have included lymph node enlargement and pleural effusion. In our study, the former was more common in patients with miliary metastases than in those with tuberculosis (p < 0.05), a difference which could help distinguish the two conditions. Hong et al. [7] reported that pleural effusion occurred in 16% of miliary tuberculosis cases, and in our study pleural effusion occurred in three (27%) patients with miliary metastasis and three (17%) with miliary tuberculosis. There were no significant difference between the two groups in terms of coalescence or groud-glass appearance.

A limitation of this study was its retrospective design, and because of the limited number of cases, further investigation is required. There is, in addition, a need for correlative pathologic study.

In conclusion, the major points of difference between miliary metastases and miliary tuberculosis were that in the former, involvement of the interlobular septa, peribronchovascular bundle thickening, and lymph node enlargement were more frequent. These findings can help differentiate the two diseases.

References
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\[ \text{Comparison of High-resolution CT Findings between Miliary Metastases and Miliary Tuberculosis} \]

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\[ \text{Objective: To compare the high-resolution CT findings between miliary metastases and miliary tuberculosis.} \]

\[ \text{Methods: From 1998 to 2002, 5 mm high-resolution CT scans were performed on 18 patients with miliary metastases. The findings were compared with those of 11 patients with miliary tuberculosis. The findings included small nodules, ground-glass opacities, and consolidation. Chi-square analysis was used to compare the results.} \]

\[ \text{Results: The high-resolution CT findings at 1 mm were similar to those at 5 mm. The sensitivity of the findings at 1.5 mm was 81.9%, and the specificity was 64.5%. The sensitivity at 3 mm was 76.5%, and the specificity was 17.0% (p<0.001). The findings at 3 mm were significantly different from those at 11 mm (p<0.001). The findings at 3 mm were also significantly different from those at 5 mm (p<0.001).} \]

\[ \text{Conclusion: High-resolution CT findings at 1 mm are similar to those at 5 mm. The findings at 1.5 mm are more sensitive and specific than those at 3 mm (p<0.001).} \]