Miliary Tuberculosis*

Diagnostic Accuracy of Chest Radiography

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Study objective: To assess the efficacy of the chest radiograph in identifying patients with miliary tuberculosis.

Design: Retrospective case-controlled review by three independent blinded chest radiologists.

Setting: Provincial tuberculosis control center.

Patients: Population-based sample, including all proved cases of miliary tuberculosis diagnosed in the Province of British Columbia, Canada, between November 1982 and November 1992. One hundred cases of miliary tuberculosis were identified, of which 71 had chest radiographs available for review. Forty-four normal chest radiographs and 20 chest radiographs of patients with localized pulmonary tuberculosis were also included as controls.

Main outcome measures: The primary outcome of measurements was the sensitivity and interobserver variability of the chest radiograph in the diagnosis of miliary tuberculosis. The observers were also asked to describe the pattern and extent of pulmonary abnormalities based on the International Labor Organization (ILO) classification of pneumoconioses.

Results: The three independent observers identified 42, 44, and 49 of the 71 cases of miliary tuberculosis, respectively (sensitivity, 59 to 69%). The three observers incorrectly diagnosed miliary tuberculosis in 2, 0, and 2 of the 64 controls, respectively (specificity, 97 to 100%). There was good interobserver agreement (90%, kappa=0.77). The nodules measured less than 3 mm in diameter in 90% of cases in which miliary tuberculosis was correctly identified. In 10% of cases, the nodules measured greater than 3 mm in diameter. The ILO profusion scores ranged from mild (profusion score 1) in 45% of cases, through moderate (profusion score 2) in 27%, and severe (profusion score 3) in 28%.

Conclusions: The chest radiograph allowed identification of 59 to 69% of cases of miliary tuberculosis with a high specificity and good interobserver agreement. (CHEST 1996; 110:339-42)

Key words: lung diseases; lung radiography; tuberculosis, miliary; tuberculosis, pulmonary

Abbreviations: ILO=International Labor Organization; TB=tuberculosis

There is concern regarding rising rates of tuberculosis (TB), including disseminated or miliary TB, which is a more common condition in HIV infection. In addition, miliary TB is often underdiagnosed in the elderly, resulting in autopsy diagnosis of unsuspected disseminated TB.

The chest radiograph plays an important role in the initial detection and final diagnosis of miliary TB. The characteristic radiographic findings consist of a large number of nodular opacities measuring 1 to 3 mm in diameter scattered diffusely throughout both lungs. Previous studies have reported widely variable results, with miliary lesions being identified on the chest radiograph in 30 to 93% of cases. These studies were not population-based, lacked control subjects, and, with the exception of one study from South Africa, were published more than 20 years ago. The purpose of this study was to determine the efficacy of the chest radiograph in the diagnosis of miliary TB based on a review of all cases diagnosed over 10 years in the province of British Columbia, Canada, inclusion of a group of control subjects, and interpretation by three independent blinded observers.

Materials and Methods

The records from the TB registry for the Province of British Columbia, Canada, were reviewed for cases of miliary TB from November 1982 to November 1992. Only patients who had a good quality posteroanterior or anteroposterior chest radiograph as determined by an independent expert chest radiologist were included in the study. Patients with only poor quality portable radiographs (n=2), and patients without radiographs obtained prior to commencement of treatment (n=2) were excluded from the study. Of...
a total of 100 cases, chest radiographs from the time of diagnosis were available in 71 patients. In 65 cases, the radiograph consisted of a posteroanterior radiograph obtained at 70 to 115 peak kilovoltage (kVp) and in 4 cases of an anteroposterior radiograph obtained at 80 kVp. The kVp used for the radiographs in the two children included in the study is not known.

The study also included 64 control chest radiographs. The controls included 44 normal chest radiographs and 20 chest radiographs performed on patients with localized pulmonary TB. The 20 chest radiographs performed on patients with localized pulmonary TB were selected by an independent radiologist to include focal findings of TB similar to those seen in the patients with miliary TB. These 20 patients had no clinical or radiologic evidence of disseminated disease. The latter were included to prevent the observers from assuming that miliary TB was present if any abnormality was seen on the radiograph. The chest radiographs were independently reviewed in random order by three "blinded" chest radiologists. The observers were aware that the study included normal control subjects, patients with localized TB, and patients with miliary TB, but were not aware of how many cases were in each category. The observers were asked if miliary TB was evident on the radiograph and, if so, to characterize it according to the International Labor Organization (ILO) classification of pneumoconioses.16 The ILO classifies nodular disease according to size and profusion. The size classifications are as follows: p (<1.5 mm), q (1.5 to 3 mm), and r (>3 mm). The profusion scores are as follows: 0 (normal), 1 (mild, subtle but definite nodularity), 2 (moderate, clearly visible but not obscuring underlying markings), and 3 (severe, extensive nodularity obscuring underlying markings). The distribution of nodules was assessed for each of six lung zones: right and left upper lung zones, right and left mid lung zones, and right and left lower lung zones. The observers were also asked to comment on the presence of additional findings, including consolidation, cavitation, granulomas, lymphadenopathy, and pleural disease.

Sensitivity and specificity were calculated for each observer. In addition, the interobserver agreement was evaluated using the kappa statistic.17

**Results**

The study included 43 male and 28 female subjects. The patients’ ages ranged from 1 to 90 years with a mean age of 52 years and a median age of 51 years. The study population was comprised almost entirely of adults with only two patients being younger than 18 years of age. Underlying disorders were identified in 55 patients. These included AIDS (n=7), chronic renal failure (n=8), solid organ malignancies (n=8), diabetes (n=5), lymphoproliferative disease (n=5), collagen vascular disease (n=5), renal transplantation (n=1), and alcoholism (n=16). The median time interval between the date of the chest radiograph and the date of the final diagnosis was 3 days.

The diagnosis was made in 35 cases on the basis of typical radiographic findings and a positive smear or culture from a sputum sample or bronchial lavage. In 21 cases, the diagnosis was based on a positive smear or culture from multiple sources. In three cases, the diagnosis was based on typical histologic findings from liver or lung biopsy specimens. In ten cases, the diagnosis was made at autopsy. In two cases, the diagnosis was based on a combination of typical clinical labora-

<table>
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<tr>
<th>Table 1—Results*</th>
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<tr>
<td>Observer No.</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
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<td>3</td>
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*n=135 (71 patients with miliary TB, 64 control subjects). TP=true positive; TN=true negative; FP=false positive; FN=false negative.

Table 2—Distribution of Disease*

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<th>Zone</th>
<th>Right, %</th>
<th>Left, %</th>
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<tbody>
<tr>
<td>Upper</td>
<td>92</td>
<td>76</td>
</tr>
<tr>
<td>Middle</td>
<td>92</td>
<td>88</td>
</tr>
<tr>
<td>Lower</td>
<td>97</td>
<td>97</td>
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*Diffuse disease (all zones involved)=80%.

Results are given in Table 1. Of the 71 patients with miliary TB, diffuse nodular opacities were identified by the observers in 49, 44, and 42 cases giving sensitivities of 69%, 62%, and 59%, respectively. All three observers correctly identified the 37 patients who had been considered prospectively to have typical radiographic findings of miliary TB. Of the 64 control cases, 62, 64, and 62 of the radiographs were correctly read as demonstrating no evidence of miliary disease giving specificities of 97%, 100%, and 97%, respectively. Interobserver agreement was calculated at 90% with a kappa of 0.77 (p<0.0001).

Of the 49 cases with miliary TB that were correctly identified by 1 of the observers, 6 had nodules that measured less than 1.5 mm in diameter (12%), 38 had nodules that measured 1.5 to 3 mm (78%), and 5 had nodules that measured greater than 3 mm (10%). Twenty-two cases were given a profusion score of 1 (45%), 13 cases were given a profusion score of 2 (27%), and 14 cases were given a profusion score of 3 (28%).

The distribution of the nodules is given in Table 2. In most cases, nodular disease was identified in all six lung zones. Although the lower lung zones were affected slightly more often than the upper or mid zones, this was not statistically significant. Similarly, the right and the left lungs were equally affected.

Areas of consolidation were identified in 22 of 71 cases (31%). The upper lung zones were most commonly affected (17/22), followed by the lower lung zones (11/22) and mid lung zones (8/22). Cavitation was seen in only 2 of the 71 cases (3%) and calcified granulomas were identified in 9 cases (13%). Lymphadenopathy was identified on the radiograph in 11 cases (15%), including 5 with enlarged mediastinal nodes, 1 with enlarged hilar nodes, and 5 with both. The lymphadenopathy was unilateral in nine cases and
bilateral in only two. Pleural effusions were identified in 19 of the 71 cases (26%), being unilateral in 14 cases and bilateral in 5. In the subset of 7 patients with HIV infection, the 3 observers correctly identified miliary disease in 6, 5, and 5 cases, respectively (71 to 86%). The ages ranged from 31 to 73 years with a mean of 36 years. Three of these patients had enlarged lymph nodes (43%) as compared to 8 of the 64 patients who were not known to be HIV positive (13%). In the subset of 10 patients whose conditions were diagnosed only at autopsy, the observers correctly identified miliary disease in 6, 4, and 3 cases, respectively (30 to 60%). The mean age was 72 years, ranging from 33 to 79 years. While enlarged nodes were not identified in any of these patients, areas of consolidation were demonstrated in 4 cases (40%) and pleural effusions were demonstrated in 4 cases (40%).

**DISCUSSION**

The radiographic appearance of miliary TB has been described in detail. Classically, numerous small nodules of uniform size (<3 mm in diameter) are scattered throughout both lungs. Both the upper and lower lung zones are affected, although they may appear more numerous in the lower lung zones presumably due to the increased volume.4-6 Descriptions of miliary TB have not previously conformed to the ILO classification of nodular disease. As would be expected in most cases, the nodules were judged to be less than 3 mm in diameter. However, in 10% of cases, the nodules measured between 3 and 10 mm in diameter. The profusion scores were either mild or moderate in most cases (ILO profusion scores 1 or 2). However, in 28% of cases, the profusion of the nodular disease was severe enough to obscure the underlying pulmonary markings (ILO profusion score 3).

Several authors have reported their experience in identifying miliary nodules in patients with disseminated TB and have reported a sensitivity based on the chest radiographic findings ranging from 33 to 93%. All of these studies, however, were retrospective analyses that used single observers, were not population based, and did not include a group of control subjects. The sensitivity in our series was lower than most of the previous reports, ranging from 59 to 69%. Interobserver agreement among all three radiologists was excellent, measuring 90% with a kappa of 0.77 (p<0.0001). Sensitivity appeared slightly higher in patients with HIV infection (71 to 85%) and slightly lower in the patients whose conditions were diagnosed only at autopsy (30 to 60%). The discrepancy between the sensitivity in our series and the sensitivity from previous reports may largely be attributed to differences in reader bias in previous studies. It should be noted, however, that because of the relatively high prevalence of miliary disease in the study population, reader bias has not been completely eliminated and the sensitivity may therefore have been overestimated.

Previous reports have identified additional radiographic abnormalities in 32 to 47% of cases.12 These include areas of consolidation, cavitation, pleural fluid, or thickening and lymphadenopathy. In our series, the incidence of associated findings was higher, with 49 of the 71 cases (69%) demonstrating some additional abnormality. Of interest, calcified granulomas were identified in 9 cases (12%), presumably representing a residua of the primary infection. The remaining associated findings have been described previously and include consolidation, hilar or mediastinal lymphadenopathy, and pleural effusion.

Lymphadenopathy was seen more often in patients with HIV infection (43%) than in patients without known HIV infection (13%). In the elderly subset of patients whose conditions were diagnosed only at autopsy, lymphadenopathy was not seen. However, consolidation and pleural effusions were identified frequently.

This report emphasizes the difficulties in diagnosing miliary TB with 10 of 71 cases (14%) being diagnosed only at autopsy. The high specificity and moderate sensitivity of the chest radiograph in identifying miliary TB highlights the need to look beyond the chest radiograph for confirmation of the diagnosis. Changes in the early stages may be subtle and alternate sources to the lung, such as blood, bone marrow, or liver biopsy, should be sought if miliary TB is suspected. Several recent studies have demonstrated that high-resolution CT can be helpful in the assessment of patients with focal and disseminated pulmonary TB.18-21 High-resolution CT consists of thin sections (1 to 2 mm) optimized by using a high-spatial frequency (edge-enhancing) reconstruction algorithm. High-resolution CT has been shown to be superior to the chest radiograph in the detection and characterization of subtle parenchymal abnormalities. CT can also be helpful in the assessment of mediastinal lymphadenopathy.22 The finding of low attenuation necrotic mediastinal lymph nodes, with rim enhancement following IV contrast infusion, strongly suggests a diagnosis of TB both in immunocompetent patients and in patients with AIDS.22,23 High-resolution CT, therefore, is recommended in the assessment of patients with suspected miliary TB who have normal or equivocal radiographic findings.

**CONCLUSION**

We conclude that the chest radiograph allows identification of 59 to 69% of cases of miliary TB with a high specificity and good interobserver agreement. Because
of the relatively low sensitivity, when this diagnosis is suspected, alternate sources to the lung should be sought for confirmation.

ACKNOWLEDGMENT: We would like to thank Dr. Ted Allan, formerly Provincial Director of TB Control BC, for facilitating access to the charts and radiographs and the Registry staff of TB Control for obtaining the records.

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