Pulmonary Disease Associated with Pleural "Asbestos" Plaques*

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The diagnosis of asbestos-related pulmonary disease is frequently based in part on the identification of pleural plaques; however, postmortem observations have suggested that pleural plaques may occur without associated pulmonary disease. To examine this issue, we compared the pulmonary parenchymal pathology in 93 patients with pleural plaques to 93 control patients matched for age, race, and sex, all autopsied at The Johns Hopkins Hospital between Jan 1, 1981 and March 31, 1986. Pulmonary sections were graded without knowledge of the patient's group for peribronchiolar fibrosis, other types of fibrosis, emphysema, and pleural changes. Correlations were found between the presence of pleural plaques and peribronchiolar fibrosis (p<0.001), alveolar fibrosis (p<0.05), large scars (p<0.02), scar-related emphysema (p<0.005), and pleural thickening (p<0.005). A history of smoking was also associated with pleural plaques (p<0.05). Interstitial fibrosis was not significantly different between the two groups. Peribronchiolar fibrosis was neither universally nor exclusively present in patients with pleural plaques, being found in 49 (53 percent) of 93 subjects with and 36 (39 percent) of 93 subjects without plaques. The results suggest that caution must be exercised in extrapolating from the identification of pleural plaques to a diagnosis of asbestos-related pulmonary disease.

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HRCT = high-resolution computerized tomography

The term, asbestos, refers to a family of fibrous hydrous minerals that possess unique tensile strength and thermal and chemical stability. Due to the unique thermal stability of asbestos, products containing asbestos have been widely used in a variety of industries, particularly in shipbuilding. The association of exposure to asbestos with pulmonary fibrosis, termed asbestosis, is now well recognized and constitutes one of the major complications of the use of asbestos.

The clinical diagnosis of asbestosis is based on a constellation of nonspecific clinical findings. These findings include the presence of dyspnea and a nonproductive cough, a history of substantial exposure to asbestos, a restrictive pattern on pulmonary function tests, and small linear opacities and pleural plaques on the chest roentgenogram. Out of all of these findings, the greatest significance is often placed on the presence of pleural plaques. Increased public awareness and litigation for personal injury associated with exposure to asbestos has heightened the need for early and accurate diagnostic tests for asbestosis.

High-resolution computerized tomography provides detailed images of pulmonary parenchyma, and it has therefore been hypothesized that HRCT can be used to detect early asbestosis. The purpose of this study is twofold: (1) to examine the significance of the presence of pleural plaques in the diagnosis of asbestosis; and (2) to examine, through a detailed study of the pulmonary pathologic findings associated with pleural plaques, whether or not there is a morphologic basis for diagnosing asbestosis radiographically.

Materials and Methods

The postmortem files of The Johns Hopkins Hospital were searched for cases in which pleural plaques (Fig 1) were identified at autopsy. Autopsies performed between Jan 1, 1981 and March 31, 1986 were selected for study. Ninety-three autopsies were identified in which pleural plaques were present and in which histologic sections of pulmonary parenchyma were available for study. Ninety-three autopsies of patients matched for age, race, and sex, on whom there was no history of asbestos exposure or pleural plaques, were selected as controls. As with the cases with pleural plaques, all patients used as controls were autopsied at The Johns Hopkins Hospital between Jan 1, 1981 and March 31, 1986.

All available pulmonary histologic findings were reviewed by three of us (R.F.S., R.H.H., and C.M.H.). A mean of eight slides was examined for each patient. Pulmonary sections were graded without knowledge of the patient's group for peribronchiolar fibrosis, other types of fibrosis, emphysema, and pleural change. The degree of peribronchiolar fibrosis (Fig 2A) was scored from 0 to 12 based on the scheme for grading asbestosis established by the Pneumoconiosis Committee of the College of American Pathologists and the National Institute of Occupational Safety and Health in 1982. The score is the product of two grades, one for severity (scored 0 to 4) and the other for extent of involvement (scored 1 to 3). Other

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Pulmonary Disease Associated with Pleural Asbestos Plaques (Sison et al).

Figure 1. Pleural plaques, which have been considered to be hallmarks of exposure to asbestos, are composed of relatively acellular hyalinized collagen (hematoxylin-eosin, original magnification ×10).

Figure 2 A (top). Peribronchiolar fibrosis with associated anthracosis in control patient. Peribronchiolar fibrosis was neither universally nor exclusively present in patients with pleural plaques. B (bottom). Alveolar fibrosis, characterized by fibrosis involving alveolar spaces (organizing pneumonia), was more common in patients with pleural plaques (hematoxylin-eosin, original magnification ×75).

Figure 3 A (top). Interstitial fibrosis was seen in both cases with pleural plaques and control patients. In this case, fibrosis appeared to be secondary to deposition of iron in an arc welder. B (bottom). In contrast to interstitial fibrosis, large-scar fibrosis obliterates underlying pulmonary architecture (hematoxylin-eosin, original magnification ×75).

Types of fibrosis (alveolar, interstitial, and large scar) were each graded on a scale of relative severity ranging from 0 to 4 (least to greatest). Alveolar fibrosis (Fig 2B) was defined as fibrosis primarily involving the alveolar spaces (organizing pneumonia). Interstitial fibrosis (Fig 3A) was defined as fibrosis sparing the air spaces and predominantly involving the alveolar walls and interlobular septa. Large scar fibrosis (Fig 3B) was defined as fibrous bands obliterating the underlying pulmonary architecture. The relative degrees of pleural thickening and of centrilobular and scar-related emphysema were graded on a scale from 0 to 3 (least to greatest). The presence or absence of asbestos bodies was noted. The paired t-test or the χ² test was used in all statistical analyses.

Results

Demographics

The studied group included 82 men and 11 women, 60 whites and 33 blacks, and their ages ranged from 25 to 91 years of age (mean, 65 years) (Table 1). Fifty-six of these patients had a history of cigarette smoking documented in their postmortem records. Eighteen had primary pulmonary neoplasms, and 12 had pul-
monary metastases from extrapulmonary malignancies. Seventeen had received radiation therapy, and 16 had had chemotherapy. Of the control patients, 42 were smokers. Nine had primary pulmonary neoplasms, and 12 had metastases to the lung. Eighteen had undergone radiation therapy, and 20 had received chemotherapy.

**Histologic Features of the Lungs**

**Fibrosis:** Peribronchiolar fibrosis was identified in 49 (53 percent) of the 93 patients with pleural plaques and in 36 (39 percent) of the 93 control patients (Table 2). The mean peribronchiolar fibrosis product in the group with pleural plaques (1.45) was significantly (p<0.001) greater than that in the control group (0.68). Peribronchiolar fibrosis product was not significantly different for patients with and without a smoking history.

The relative degrees of alveolar, interstitial, and large scar fibrosis were also evaluated. Alveolar fibrosis (organizing pneumonia) was identified in 22 of the cases with pleural plaques (mean score, 0.39) and in 11 of the control cases (mean score, 0.17). This difference was significant (p<0.05). Similarly, the degree of large scar fibrosis was also more severe in the patients with pleural plaques (p<0.02) than in the controls. Large scar fibrosis was identified in 38 of the control patients (mean score, 0.56), while 53 of the cases with pleural plaque had large scars (mean score, 0.85).

Differences in interstitial fibrosis were, however, not significant. Sixteen of the control cases (mean score, 0.24) and 22 of the cases with pleural plaques (mean score, 0.40) showed this change.

**Emphysema:** The relative degrees of centrilobular and scar-related emphysema were graded in each case, with the understanding that emphysema is difficult to diagnose on histologic grounds alone when the sections are not prepared from lungs fixed in distention. Centrilobular emphysema was seen in both cases and controls with about equal frequency (32 cases and 28 cases, respectively), and the degree of centrilobular emphysema present in these cases was not significantly different (mean score of 0.46 vs 0.45). In contrast, scar-related emphysema was more common in the cases with pleural plaques (21 cases) than the controls (nine cases), and scar-related emphysema was more severe (mean score of 0.31 vs 0.12) in the cases with pleural plaques. This difference was statistically significant (p<0.02).

**Pleural Changes:** Pleural thickening was more common in the cases with pleural plaques (35 patients) than in the controls (18 patients) and more severe (mean score of 0.74 vs 0.32, p<0.005).

**Asbestos Bodies:** Asbestos bodies were identified in routine histologic sections in eight of the cases with pleural plaques. In six of these cases, peribronchiolar fibrosis was also present (Fig 4). By definition, these six cases fulfill criteria for the diagnosis of asbestosis. The other pulmonary pathologic findings present in these six cases of asbestosis included pleural thickening (four cases), large scar (three cases), alveolar fibrosis

### Table 1—Demographic Features*

<table>
<thead>
<tr>
<th>Data</th>
<th>Patients with Pleural Plaques</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>Mean age, yr</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Race (white/black)</td>
<td>60/33</td>
<td>60/33</td>
</tr>
<tr>
<td>Sex ratio (male/female)</td>
<td>82/11</td>
<td>82/11</td>
</tr>
<tr>
<td>Primary pulmonary neoplasms</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Pulmonary metastases</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Radiation therapy</td>
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<td>18</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>Smoking</td>
<td>56</td>
<td>42</td>
</tr>
</tbody>
</table>

*Data are numbers of subjects.

### Table 2—Comparison of Pulmonary Parenchymal Pathologic Findings

<table>
<thead>
<tr>
<th>Histologic Feature</th>
<th>93 Patients with Pleural Plaques</th>
<th>93 Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Grade of All Cases</td>
<td>No. Positive</td>
<td>Mean Grade of All Controls</td>
</tr>
<tr>
<td>Peribronchial Fibrosis</td>
<td>49</td>
<td>1.45</td>
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<tr>
<td>Pleural thickening</td>
<td>35</td>
<td>0.74</td>
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<tr>
<td>Asbestosis†</td>
<td>6</td>
<td>0.30</td>
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<tr>
<td>Large scar fibrosis</td>
<td>33</td>
<td>0.59</td>
</tr>
<tr>
<td>Scar-related emphysema</td>
<td>21</td>
<td>0.31</td>
</tr>
<tr>
<td>Alveolar fibrosis</td>
<td>22</td>
<td>0.39</td>
</tr>
<tr>
<td>Interstitial fibrosis</td>
<td>22</td>
<td>0.40</td>
</tr>
<tr>
<td>Centrilobular emphysema</td>
<td>32</td>
<td>0.46</td>
</tr>
</tbody>
</table>

*NS, Not significant.
†Defined as peribronchiolar fibrosis associated with asbestos bodies.
changes in the chest roentgenogram include fine linear and irregular opacities in the lower pulmonary fields which progress to honeycombing of the lung; however, these findings are nondiagnostic, and a variety of other interstitial pulmonary diseases may give this same appearance. Nonetheless, medical and legal decisions are based on the interpretation of these radiographic abnormalities. It was hoped that CT and, in particular, HRCT would help resolve this dilemma and that the diagnosis of asbestosis could be firmly established by CT. Early clinical studies on relatively small populations of patients concluded that CT was able to detect early fibrosis, even when the findings from conventional roentgenograms and pulmonary function tests were normal or inconclusive. The signs on CT purported to have an association with asbestosis included (1) thickening of septa, (2) parenchymal linear densities, (3) subpleural dependent density, (4) curvilinear subpleural lines, (5) honeycombing, and (6) pleural thickening.

The purpose of this study was to examine the pathologic findings associated with pleural plaques, in order to determine what significance the presence of pleural plaques should be given in establishing the diagnosis of asbestosis, and to search for histologic changes associated with exposure to asbestos which might be detected radiographically.

We found that while the presence of pleural plaques was associated with peribronchiolar fibrosis, a significant percentage (47 percent; 44/93) of the patients with pleural plaques did not have peribronchiolar fibrosis. Indeed, peribronchiolar fibrosis with associated asbestos bodies (asbestosis) was found in only 6 percent (6/93) of the patients with pleural plaques. Pleural plaques therefore cannot be used as an absolute marker of parenchymal disease.

While not diagnostic for asbestosis, the presence of pleural plaques was highly correlated with peribronchiolar fibrosis, large scars, pleural thickening, organizing pneumonia, and scar-related emphysema. The presence of pleural plaques has itself been shown to be correlated with exposure to asbestos. Our findings of an association between these various forms of pulmonary fibrosis and pleural plaques therefore confirms previous studies which have implicated asbestos as a cause of pulmonary fibrosis. The higher incidence of smoking in patients with pleural plaques may also contribute to the higher incidence of pulmonary pathologic findings seen in those patients.

Each form of pulmonary fibrosis associated with pleural plaques can be expected to have a distinct appearance on HRCT; for example, peribronchiolar fibrosis should be manifested by increased radiodensity in the centrilobular areas, and scar-related emphysema should be seen by an area of high attenuation adjacent to an area of low attenuation.
Although a strong association was found between these forms of fibrosis and pleural plaques, no single morphologic finding was exclusively present in the patients with pleural plaques; for example, peribronchiolar fibrosis was present in 39 percent (36/93) of the patients without plaques. This result is not entirely surprising, as peribronchiolar fibrosis, although associated with asbestosis, can be caused by smoking.23 These results suggest that radiologists should not seek a single "sign" by which to diagnose asbestosis, but rather should use radiography to evaluate the extent of pulmonary parenchymal disease, with the understanding that several disease processes may cause the same findings.

This conclusion is supported by recent case reports in which overreading of roentgenograms and scans from CT led to an erroneous diagnosis of asbestosis. Collins et al.,24 in a review of 45 scans from CT in asbestos workers, presented a case in which pulmonary sarcoidosis was diagnosed as asbestosis. Similarly, Pilate et al.25 have reported the subpleural curvilinear shadow on CT in patients with no known history of pulmonary disease.

While this study suggests that the diagnosis of asbestosis should not be based solely on radiographic findings, the possibility that focal nonspecific pathologic findings might combine to form patterns unique to asbestosis cannot be ruled out. Detailed pathologic-radiographic correlations, such as can be established with inflation-fixed lungs,24 would be the best method for detecting these patterns.

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REFERENCES

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