Mycosis fungoides Presenting as ARDS and Diagnosed by Bronchoalveolar Lavage*

Radiographic and Pathologic Pulmonary Manifestations

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A patient with Mycosis fungoides involving the lung, presenting with ARDS, and diagnosed by bronchoalveolar lavage, is described. A review and correlation of chest radiographic manifestations and pathologic observations are presented. We stress the importance of obtaining a specific diagnosis in light of the tenuous radiographic-pathologic correlation and discuss procedures for diagnosis and the inclusion of bronchoalveolar lavage as a previously undescribed diagnostic modality. The dismal prognosis of these patients, once pulmonary involvement is diagnosed, is noted.

*Mycosis fungoides is a slowly progressive malignant disorder, initially manifest as skin disease, with a fatal outcome. First noted in 1805, Alibert believed it a manifestation of yaws, but now it is described as one of a number of cutaneous T-cell lymphoma syndromes. Due to the initial indolent presentation and apparent lack of aggressive spread, early authors held this to be solely a cutaneous disorder, without systemic involvement. This view was perpetuated for many years until a number of more recent autopsy series exposed the common nature of the systemic spread of this malignancy.

Pulmonary involvement in this disorder has been noted in anecdotal reports. However, chest radiographic manifestations have never been correlated meticulously with pathologic observations. Although a variety of pulmonary presentations have been noted, no patient with Mycosis fungoides has presented with the adult respiratory distress syndrome (ARDS). The purpose of this article is to report a case of Mycosis fungoides with ARDS, review the pulmonary radiographic and pathologic manifestations, and discuss diagnostic procedures and implications based on these observations.

Case Report

A 34-year-old black man came to medical attention in August 1984, complaining of a lump in the left groin. Physical examination revealed small bilateral axillary and inguinal adenopathy. A chronic skin rash of several years’ duration, unresponsive to conservative treatment, also was noted. Biopsies of the rash and a left inguinal

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FIGURE 1. Admission A-P chest radiograph displaying a full mediastinum, vague nodular densities, and patchy diffuse alveolar filling. Node revealed Mycosis fungoides. Staging included negative results of chest radiograph, abdominal CT scan, and bone marrow aspirate and biopsy. A blood buffy coat smear revealed no Sezary cells. A 44Ca scan displayed hilar nodal uptake; however, this information was not utilized in determination of treatment. Topical nitrogen mustard treatment was initiated with moderate control of his disease over the next seven months. Five days prior to admission he developed fever and diarrhea, followed by a cough productive of mucoid sputum. Shortness of breath prompted an emergency room visit. On examination he was tachypneic, afibrile, and had bilateral ronchi. He was hypoxemic (room air arterial blood gas levels: pH 7.43, PaCO2 33 mm Hg; PaO2 49 mm Hg), and a chest radiograph showed mediastinal fullness, vague nodular densities, and patchy alveolar filling (Fig 1).

On referral to the Medical University of South Carolina, he was alert, without overt signs of heart failure, and had a palpable spleen tip. The previously reported peripheral adenopathy was unchanged. White blood cell count was 19,300/μl with 79 PMN, 7 bands, 10 lymphs, and 4 monos. Hematocrit was 53 volumes % and prothrombin time 15/12 seconds (patient/control). Gram stain of the sputum revealed numerous PMNs, but no organisms. Diagnostic considerations included opportunistic infection in a patient with underlying malignancy, hydrostatic vs capillary leak pulmonary edema, or tumor invasion of the lung. A bronchoalveolar lavage (BAL) was performed without transbronchial lung biopsy (TBLB) due to his coagulopathy. Five 50 ml aliquots of normal saline solution were instilled into the right middle lobe bronchus with the bronchoscope wedged to promote optimum fluid return. Approximately 50 percent

FIGURE 2. Bronchoalveolar lavage cytology specimen (400 × ) showing typical Sezary cells (arrow).
of the fluid was recovered on aspiration and sent for special bacteriologic stains and cultures; results were negative. Approximately 100 ml of fluid was sent for cytologic analysis. This fluid was centrifuged and from the resultant pellet a cell block prepared. It was stained with a modified Papanicolaou preparation using hematoxylin and eosin, and examined cytologically. Swan Ganz catheter insertion revealed PCWP of 13 mm Hg; CO, 2.3 L/min; and SVR, 1,450 dynsec/cm². The patient was ventilated with static compliances of 18-22 ml/cm H₂O. Arterial blood gas levels on IMV 18, FiO₂ 1.0, Vt 900 ml, were: pH, 7.34; PaCO₂, 36 mm Hg; PaO₂, 100 mm Hg. Despite therapy with mechanical ventilation, hemodynamic support, and antibiotics, he died in less than 24 hours. At the time of death, BAL fluid was read as positive for Sezary cells (Fig 2). Autopsy revealed diffuse visceral organ involvement and bilateral tumor involvement of the lungs on gross examination. Both lungs were heavy and edematous, the right and left lungs weighing 1,370 g and 1,330 g respectively. Each was extensively infiltrated with beige tumor nodules (Fig 3). The hilar and mediastinal nodes were enlarged and also contained tumor. There was no area on gross examination consistent with pneumonia. Microscopically, the lungs were diffusely infiltrated with tumor cells including interstitial and alveolar components (Fig 4). Dense collections centered about septa, bronchi, arteries and veins, and tumor invasion into the pulmonary veins was noted. Hyaline membrane formation and fibrin deposition were noted, but no area of pneumonia or infarction was seen. Other organs involved were the right atrium, both adrenals, colon, left ureter, liver and kidneys.

**DISCUSSION**

This case is unusual in several respects. The young age at diagnosis (35 years) is 16 years less than the average reported age of 51 years.8-3 The short duration of his diagnosed illness (seven months) is much less than the 3.3 year average noted by Rappaport4 for patients initially diagnosed with extracutaneous involvement. The rapid spread of his disease, although reported, is uncommon. The chest radiographic and clinical presentation, patchy nodules and alveolar filling producing ARDS, has not been reported previously. This patient met criteria for the syndrome, ie, acute respiratory distress, diffuse alveolar infiltrates on chest radiograph, large A-a gradient for oxygen unresponsive to high inspired fractions of oxygen, decreased compliances, and normal PCWP. Reports of consolidation13 and one of alveolar filling12 exist, but these patients did not present in respiratory failure. The method of diagnosis, bronchoalveolar lavage, is unique in this setting. One report of diagnosis by sputum cytology20 has been noted, but all other diagnoses have been established by TBLB, open lung biopsy, pleural fluid cytology and pleural biopsy, or at autopsy.1,7,11,13,14

Pathologic description of pulmonary abnormalities in *Mycosis fungoides* have been published.1,7,10,13 In general, the lung is involved in 50-70 percent of autopsy cases. Table 1 lists several autopsy series and pathologic changes noted on gross or microscopic examination of the lung. As seen in Table 1, the pathologic changes included parenchymal nodules, enlarged mediastinal nodes, pulmonary infiltrates, and pleural effusions.1,7,9

The chest radiographic manifestations of this disorder have been described by several authors.7,15 The most common

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**Table 1—Pathologic Pulmonary Involvement in Mycosis Fungoides**

<table>
<thead>
<tr>
<th>No. Cases with Gross Lung Involvement</th>
<th>Gross Findings</th>
<th>Microscopic Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rappaport4</td>
<td>32</td>
<td>18</td>
</tr>
<tr>
<td>Long, et al5</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Robbins,6</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Epstein5</td>
<td>66</td>
<td>42</td>
</tr>
<tr>
<td>Edgcomb1</td>
<td>17</td>
<td>Mediatinal nodes, pleural effusions, infiltrates</td>
</tr>
</tbody>
</table>

NR = not reported
finding in these 44 patients was a normal chest radiograph (17) followed by nodules (nine) hilar or mediastinal adenopathy (eight) and interstitial infiltrates (eight). Three cases of pleural effusions and two cases of focal alveolar filling or consolidation were noted.

Of the above mentioned studies of pathologic and radiographic changes in pulmonary Mycosis fungoides, only six actually correlate radiographic changes with pathologic material. In the report of Lehrer et al., a TBLB of a radiographic nodule was positive for clusters of Mycosis fungoides cells. Israel's report of a rapidly progressive radiographic infiltrate was confirmed on autopsy as massive tumor involvement of the lung. Robbins report of bilateral nodules included one which was verified at autopsy. In the report by Margolin et al., two infiltrates were confirmed at autopsy, six nodules by sputum cytology (one), open lung biopsy (three) or autopsy (two), and two of three pleural effusions were identified by cytology or biopsy. All infiltrates or nodules noted in the three cases of Wolfe et al. were present pathologically, but hilar adenopathy, present on autopsy, was not identified radiographically. In their series of 15 patients, Long and Mihm noted four cases of hilar adenopathy, but on autopsy the 13 had mediastinal adenopathy and eight had pulmonary infiltrates.

Overall, there appears to be a relationship between what is seen radiographically and pathologically in Mycosis fungoides. Although an area of abnormality on chest radiograph tends to show tumor pathologically, a normal chest radiograph does not rule out pathologic involvement. Furthermore, an area of radiographic abnormality cannot be assumed to be pulmonary Mycosis fungoides. Despite the appropriate clinical setting, one must aggressively pursue a specific diagnosis in patients with radiographic abnormalities since they lack specificity or sensitivity for Mycosis fungoides and could represent opportunistic infections, primary lung or metastatic carcinoma, drug reaction, pulmonary infarction, radiation pneumonitis, congestive heart failure or noncardiogenic pulmonary edema. The rapidity of radiographic progression should not lead to an assumption of infection as seen in the present case and the report by Israel.

Although the necessity of establishing a diagnosis is obvious, one should not immediately proceed to open lung biopsy unless pressed by the patient's clinical condition on presentation. Prior reports note establishment of diagnosis by sputum cytology, TBLB, and by pleural fluid and biopsy analyses. In this case, bronchoalveolar lavage proved diagnostic, displaying tumor cells in the lavage fluid without any evidence of infection. Others have shown the utility and safety of bronchoalveolar lavage in the diagnosis of opportunistic infection or tumor when TBLB is contraindicated by a coagulopathy. In this case, the recovered fluid revealed Sezary cells. These cells, pathognomonic of Mycosis fungoides in the appropriate clinical setting, resemble medium-sized lymphocytes, with large convoluted or cerebriform nuclei and a narrow rim of cytoplasm containing vacuoles. These cells have T-cell characteristics, including E-rosette formation, and display helper cell activity about 50 percent of the time. If these less invasive measures are unsuccessful, open lung biopsy is generally positive in an area of radiographic abnormality.

Once the diagnosis of pulmonary involvement is established the prognosis is poor. In general, biopsy-proven visceral involvement is predictive of less than three months' survival, and the prognosis with pulmonary involvement is even more dismal. Some reports suggest that survival is measured in days to weeks once histologic proof of pulmonary Mycosis fungoides is obtained.

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