knowledge, to show gross pericardial calcification in the roentgenograms. Pericardial calcification is probably related to the duration of pericarditis, and it is possible that, in our patient, the disease may have been undetected for some years. Microscopic calcification was previously noted in pericardial specimens obtained from a patient with "rheumatoid pericarditis." The possibility of tuberculous or other infective etiology has been excluded in our patient; he had a history of sarcoidosis and lupus erythematosus.

The pericardial effusion was consistent with rheumatoid synovitis. Arthritis Rheum 13:713-723, 1970

## Table 1—Hemodynamic Findings Before and After Surgery

<table>
<thead>
<tr>
<th>Cardiac Catheterization Data</th>
<th>Before Surgery</th>
<th>After Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressures (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right atrium</td>
<td>a=20</td>
<td>a=10</td>
</tr>
<tr>
<td>Left atrium</td>
<td>v=22</td>
<td>v=10</td>
</tr>
<tr>
<td>Mean</td>
<td>mean=16</td>
<td>mean=6</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>38/18</td>
<td>32/10</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>38/22</td>
<td>23/10</td>
</tr>
<tr>
<td>Pulmonary artery wedge</td>
<td>a=20</td>
<td>a=14</td>
</tr>
<tr>
<td></td>
<td>v=14</td>
<td>v=11</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>112/20</td>
<td>100</td>
</tr>
<tr>
<td>Femoral artery</td>
<td>142/77</td>
<td></td>
</tr>
<tr>
<td>Left ventricular volumes, ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic volume</td>
<td>102.5</td>
<td></td>
</tr>
<tr>
<td>End-systolic volume</td>
<td>66 ml/M²</td>
<td></td>
</tr>
<tr>
<td>Stroke volume</td>
<td>40.6</td>
<td></td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>66.6</td>
<td></td>
</tr>
<tr>
<td>Cardiac output</td>
<td>4.7 liter/min</td>
<td></td>
</tr>
<tr>
<td>Heart rate</td>
<td>90 beats/min</td>
<td></td>
</tr>
<tr>
<td>Stroke volume</td>
<td>53 ml</td>
<td></td>
</tr>
<tr>
<td>Resistance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total systemic resistance</td>
<td>1980 (21 units)</td>
<td></td>
</tr>
<tr>
<td>Pulmonary vascular resistance</td>
<td>200 (2.5 units)</td>
<td></td>
</tr>
<tr>
<td>Blood gases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A-V O2 difference</td>
<td>3.8 volume %</td>
<td></td>
</tr>
</tbody>
</table>

A 58-year-old woman, treated with busulfan for chronic myelogenous leukemia, developed diffuse interstitial pulmonary infiltrates. Histopathologic changes seen in busulfan lung were demonstrated by transcatheter biopsy, and later confirmed at autopsy. This case further illustrates the diagnostic usefulness of transcatheter pulmonary biopsy.

**Busulfan** has been used for over 20 years in the treatment of chronic myelogenous leukemia. This drug has respiratory side effects, referred to as "the busulfan lung syndrome," that include bronchial and alveolar lining cell atypia, intra-alveolar and interstitial fibrosis, and the variable clinical symptoms of fever, weight loss, dyspnea, and tachypnea. Associated cellular atypia is often found in endocervical glandular epithelium, renal tubular cells and pancreatic acinar cells at autopsy. The cytologic diagnosis of busulfan effect has been made on sputum samples and cervical smears. With cytologic techniques, however, one is limited to interpretation of the cytologic appearance of the tissue sample.

**References**


**Diagnosis of Busulfan Lung by Transcatheter Biopsy**

*Russell K. Brynes, M.D.,** S. Hassan Mostafavi, M.D.;† John J. Fennessy, M.D.,; and Daiva Varakojis, M.D.‖*

A 58-year-old woman, treated with busulfan for chronic myelogenous leukemia, developed diffuse interstitial pulmonary infiltrates. Histopathologic changes seen in busulfan lung were demonstrated by transcatheter biopsy, and later confirmed at autopsy. This case further illustrates the diagnostic usefulness of transcatheter pulmonary biopsy.

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This work was supported in part by USPHS Grant CA 8970-06
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tation of cellular atypia, and evaluation of the extent of interstitial pulmonary fibrosis is not possible. Despite the symptomatic relief offered by steroid therapy, the syndrome often ends in terminal respiratory failure.$^6$-$^8$

The hazards of percutaneous needle biopsy, transbronchoscopic biopsy, and open biopsy of the lung are well known.$^6$-$^8$ Transcatheter bronchial brushing and forceps biopsy under fluoroscopic control permit a safer selective sampling of tissue from peripheral as well as central pulmonary lesions.$^8$

In the case to be discussed here, morphologic changes consistent with a diagnosis of busulfan lung were confirmed by transcatheter biopsy, and autopsy.

**CASE REPORT**

A 58-year-old Mexican woman was known to have had chronic myelogenous leukemia since 1968. She was treated with busulfan, 2-4 mg per day, for three years. During an admission in February, 1972, hepatosplenomegaly and fibrous replacement of bone marrow were demonstrated. In May, 1972, the patient developed frequent elevations in temperature, with a nonproductive cough. A chest x-ray film two weeks later (Fig 1) showed a patchy infiltration in the right upper lobe and interstitial infiltrates throughout both lung fields. On admission to our hospital in July, 1972, the patient had a persistent dry cough and tachypnea (24 respirations/min). The spleen extended 11 cm below the left costal margin, and the total liver span was 14 cm by percussion.

The white blood cell count was 70,000 cu/mm with 15 percent neutrophils, 14 percent bands, 13 percent metamyelocytes, 19 percent myeloblasts, 3 percent eosinophils, 1 percent basophils, and 5 percent lymphocytes. Hematocrit was 22.6 percent, hemoglobin 7.9 gm percent, and the platelet count was 705,000 cu/mm. The peripheral blood smear showed marked polychromasia, hypochromasia, anisocytosis and poikilocytosis, with 36 nucleated red cells/100 white cells and many giant platelets with bizarre shapes. Leukocyte alkaline phosphatase was 326/100 neutrophils (normal value: 43-123/100 neutrophils). A bone marrow aspiration yielded a dry tap. Core biopsy of iliac crest bone marrow was interpreted as compatible with myelosclerosis with myeloid metaplasia. Karyotype analysis on material obtained from the bone marrow biopsy revealed the presence of the Philadelphia chromosome. Chest x-ray films demonstrated bilateral underinflation of the lungs with diffuse interstitial infiltrates.

To define the nature of the pulmonary infiltrates further, and to exclude the clinical suggestion of opportunistic infection, we performed transcatheter forceps and brush biopsies. Histopathology of the forceps biopsy (Fig 2) revealed diffuse interstitial and intra-alveolar fibrosis. The alveoli and bronchioles were lined by large cells with hyperchromatic nuclei, and variable amounts of eosinophilic cytoplasm. Similar large atypical cells were found in histologic sections of the brush biopsy. The diagnosis of pulmonary fibrosis with atypical alveolar and bronchiolar lining cells, consistent with busulfan lung, was made. Cultures from the bronchial washings grew *Serratia marcescens*, *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Diplococcus pneumoniae*. Treatment was instituted with gentamicin and methicillin, but respiratory difficulties continued and the patient died in respiratory failure on the 17th day of hospitalization.

Autopsy findings revealed moderate hepatomegaly (2,000 gm) with leukemic infiltration and massive splenomegaly (1,700 gm) with numerous infarcts and leukemic infiltrates. The pleural surfaces of both lungs were thickened and dark red. Cut surfaces showed multiple focal pale areas of fibrosis which were scattered throughout the parenchyma of all lobes, but were most prominent at the lower anterior border of the left upper lobe (Fig 3). Microscopically, atypical alveolar lining cells, as well as interstitial and intra-alveolar fibrosis similar to that found in the transcatheter forceps...
bacterial pathogens, and appropriate antibiotic therapy was instituted. Similarly, the presence of fungal and parasitic opportunists was excluded.

Transcatheter biopsy has been of importance not only in the diagnosis of neoplasms and infections, but also in the detection of other complications resulting from intensive chemotherapy.

ACKNOWLEDGMENT: We wish to thank Dr. J Heydemann of Ingalls Memorial Hospital, Harvey, Ill., for providing x-ray films of the patient.

REFERENCES


Figure 3. Gray area in left upper lobe represents extensive pulmonary fibrosis.

Alphal-Antitrypsin deficiency (60 mg/100 ml) and lowered trypsin inhibitory capacity (TIC) (0.12 mg/ml) was associated with a severe chronic obstructive lung disease.

Alpha1-Antitrypsin Deficiency in a Child with Chronic Lung Disease

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