DISCUSSION

Hemoptysis may occur with nephritis in a variety of diseases, such as Wegener's granulomatosis, uremic pneumonia, and periarteritis nodosa. In Goodpasture's syndrome, distinct pathologic findings in the lungs and kidneys differentiate this condition from others.

Maddock and associates\(^7\) reported immediate cessation of pulmonary hemorrhage in patients with Goodpasture's syndrome after total nephrectomy. Cleveland and co-workers\(^8\) reported a patient with Goodpasture's syndrome who was surviving six months after kidney transplantation and Freeman et al\(^9\) also reported a case of this disease in which pulmonary hemorrhage stopped after steroid therapy. They also reported prolonged survival with chronic hemodialysis. In the review by Proskay et al\(^9\), the mean time of survival in 28 of 36 patients receiving steroids was 12.7 months.

These reports suggest that extirpation of the kidney as the cause of pulmonary hemorrhage might play a role in amelioration of the condition of the patients and cessation of pulmonary hemorrhage, although fulminating hemorrhage may occur even after successful nephrectomy or dialysis. Baxter and Goodman,\(^10\) and Sheer and associates,\(^11\) speculated on the antigen similarity between alveolar and glomerular basement membrane and the ability to cause glomerulonephritis with antilung antiserum in animals. Sturgill and associates\(^11\) have used fluorescent antibody technique and were able to localize immune reaction components, gamma C globulin and beta-1 C globulin in glomerular capillary and alveolar capillary basement membrane and confirmed the above hypothesis.

Reports of others confirm the ineffectiveness of corticosteroids and immunosuppressive agents. Our observation in this patient confirms that steroids and immunosuppressive drugs may ameliorate the symptoms and even stop hemoptysis temporarily, but chronic hemodialysis and nephrectomy may be the only effective therapy in the case of Goodpasture's syndrome.

REFERENCES


Distinctive Ultrastructural Findings in a Case of Idiopathic Interstitial Pneumonia*

Paul A. Shurin, M.D. and A. Jay Block, M.D.

A patient with chronic interstitial pneumonia was treated with steroids with excellent results. Electron microscopic examination of a lung biopsy taken before treatment showed the functional defect to be associated with a gross increase in the width of the anatomic barrier to gaseous diffusion into the blood. A peculiar sudanophilic and osmiophilic inclusion was identified in the cytoplasm of his alveolar macrophages, and it is postulated that this material, which is of obscure origin, was the primary lung irritant.

A number of diffuse lung diseases have been characterized in recent years. Among these, alveolar proteinosis,\(^1\) lymphocytic interstitial pneumonia,\(^2\) and desquamative interstitial pneumonia\(^3\) are presently of unknown etiology. A larger number of diffuse pulmonary conditions are caused by inhaled irritants or allergens. Ultrastructural findings have been reported in a number of these diseases,\(^4-10\) but have not generally been of diagnostic significance. The purpose of this report is to describe a case of idiopathic interstitial pneumonia in which unique inclusions were present in the cytoplasm of alveolar macrophages.

CASE REPORT

A 50-year-old lawyer and part-time farmer was referred to the Johns Hopkins Hospital on July 29, 1969 because of progressive dyspnea and cough. He had been well until October, 1968, when he became dyspneic while climbing a hill at a football game. Several months later, dyspnea recurred, along with a brief period of diarrhea and fever. A nonproductive cough persisted beyond the end of this illness. The cough was most severe at night and recurred intermittently.

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tently during the subsequent months. By July, 1969, he had developed exertional dyspnea which markedly limited his activity. Treatment with digoxin, diuretics and antibiotics had given no relief.

The patient had lived on an Ohio farm for many years. His recent activities had included the planting of a large number of pine seedlings, burning of brush, use of 2-4-5-T to kill tree stumps, and some hay-feeding. However, careful questioning disclosed no apparent connection between these activities and his disease. The herbicide had been dissolved in kerosene or diesel oil and brushed onto stumps. He had used no spray equipment for this or any other material. The hay was freshly mowed and stated to the physician as being dry and definitely not moldy. He had used motor oils to ignite wooden debris and thought that he might have inhaled some of the smoke. He had been taking no drugs before becoming ill; specifically, nose drops and aerosolized bronchodilators were not used. He was not a smoker.

The past history was positive only for obesity and mild arthritis with minimal deformity of the hands.

He was admitted for evaluation on August 12, 1969. His pulse rate was 68, respirations 36, blood pressure 112/70 and he was afebrile. Mild cyanosis was present while at rest. There was no neck vein distention, hepatomegaly or peripheral edema. Crackling rales, which cleared with coughing, were heard at the lung bases. Aside from the arthritic arthritis with minimal deformity of the hands and the slight cyanosis, no other significant physical findings were present. The patient’s electrocardiogram was normal. Slit lamp examination revealed no ocular abnormalities.

Needle biopsy of the liver showed slight and focal hepatocellular degeneration, but no evidence of granulomatous disease. A biopsied scalene lymph node was hyperplastic. An open biopsy of the left lung was performed on August 7, 1969. The results will be described below.

After the lung biopsy, the patient was begun on prednisone 60 mg per day orally. Within several days, the diminution in his dyspnea and cough was pronounced and exercise tolerance had increased dramatically. Repeat pulmonary function testing on August 18, 1969, after one week of prednisone treatment, (Tables 1 and 2) showed improvement in the forced vital capacity (FEV1), CO diffusing capacity and arterial oxygenation, with a persisting but mildly restrictive ventilatory defect. Reduction of prednisone dosage did not interrupt the continuing symptomatic improvement. By October 7, 1969, he was able to jog. Improvement in exercise tolerance continued despite a transient fall in the diffusing capacity. Continued clearing was noted in the chest x-ray film. When last seen on April 2, 1970, he was asymptomatic, the diffusing capacity was normal, and a mild obstructive defect was the only functional abnormality.

**Methods**

The lung biopsy specimen was fixed in formalin for light microscopy and for electron microscopy in 3 percent phosphotungstic acid buffered glutaraldehyde. Routinely processed paraffin sections were stained with hematoxylin-eosin, periodic-acid Schiff, Giemsa, Masson’s trichrome, Verhoeff and Van Gieson, Mallory’s phosphotungstic acid hematoxylin, methenamine silver, Kinyon’s acid-fast, Feulgen, Gomori’s iron and pyronine.

The glutaraldehyde-fixed specimen was post-fixed in 1 percent osmium tetroxide, dehydrated in alcohol, and embedded.

**Table 1—Results of Lung Function Tests**

<table>
<thead>
<tr>
<th>Date</th>
<th>Prednisone, daily dose</th>
<th>Vital capacity, FVC</th>
<th>CO diffusing capacity</th>
<th>CO extraction</th>
<th>Tidal volume</th>
<th>Minute ventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/31/69</td>
<td>60 mg for prev. 7 d.</td>
<td>4.66 L (53%)</td>
<td>15.2 ml CO/mm Hg/min</td>
<td>40-55%</td>
<td>0.73</td>
<td>13.8 L/min</td>
</tr>
<tr>
<td>8/18/69</td>
<td>60 mg</td>
<td>2.48</td>
<td>7.2</td>
<td>25%</td>
<td>0.73</td>
<td>15.1 L/min</td>
</tr>
<tr>
<td>9/8/69</td>
<td>30 mg</td>
<td>3.93</td>
<td>16.8</td>
<td>39%</td>
<td>0.80</td>
<td>15.1 L/min</td>
</tr>
<tr>
<td>10/7/69</td>
<td>15 mg</td>
<td>4.18</td>
<td>18.9</td>
<td>42%</td>
<td>0.94</td>
<td>9.9 L/min</td>
</tr>
<tr>
<td>12/3/69</td>
<td>10 mg</td>
<td>4.18</td>
<td>10.4</td>
<td>36%</td>
<td>1.09</td>
<td>19.5 L/min</td>
</tr>
<tr>
<td>2/4/70</td>
<td>None for prev. mo.</td>
<td>4.22</td>
<td>13.6</td>
<td>32%</td>
<td>0.94</td>
<td>15.1 L/min</td>
</tr>
<tr>
<td>4/2/70</td>
<td>None for prev. mo.</td>
<td>4.44</td>
<td>15.6</td>
<td>40%</td>
<td>1.17</td>
<td>25.7 L/min</td>
</tr>
</tbody>
</table>

**Table 2—Arterial Blood**

<table>
<thead>
<tr>
<th>Date</th>
<th>Pco2 (mm Hg)</th>
<th>pH</th>
<th>Standard bicarbonate (mEq/L)</th>
<th>Po2 (mm Hg)</th>
<th>O2 Saturation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/31/69</td>
<td>30</td>
<td>7.30</td>
<td>23</td>
<td>40</td>
<td>81</td>
</tr>
<tr>
<td>8/18/69</td>
<td>30</td>
<td>7.44</td>
<td>22</td>
<td>514</td>
<td>96</td>
</tr>
</tbody>
</table>
bedded in Araldite. One micron thick sections for light microscopy were stained with methylene blue-Azure A and basic fuchsin,10 and with Sudan black for 48 hours. Grids for electron microscopy were stained with lead citrate, and examined in the RCA EMU 3G or 3H microscope.

**Results**

**Light microscopy**

The alveolar walls were characterized by increased thickness, hypercellularity and diminished vascularity (Fig 1). The alveolar epithelium was hyperplastic, with a cuboidal appearance in many areas. Cells of various types, including fibroblasts, macrophages, lymphocytes, mast cells and occasional polymorphonuclear leukocytes, had infiltrated the interstitium of the alveolar membrane. A very slight diffuse increase in connective tissue was demonstrated with special stains, and there were focal nodules of loose, young-appearing fibrous tissue. The one micron sections showed clearly that most alveolar capillaries were buried within the swollen alveolar membrane and the total volume occupied by vessels was very small. A cellular exudate composed of sheets of normal appearing alveolar macrophages and some lymphocytes, mast cells and polymorphs was present in the alveolar spaces. A few foreign body type giant cells were present in the alveolar spaces and within the tissue. Several of these contained typical asteroid bodies. No granulomata were present. A small amount of anthracotic pigment was identified, but there were no crystals or birefringent material. No organisms could be seen with special stains, and there were no viral inclusions.

In Araldite sections stained with Sudan black, spherical sudanophilic bodies could be seen in the cytoplasm of some alveolar macrophages (Fig 1, inset). In paraffin sections, these appeared as clear vacuoles of uniform size, but could not be identified with certainty. Cells containing these inclusions were quite numerous, approximately 50 such cells being present in a one micron section measuring one square mm in surface area.

**Electron microscopy**

The electron micrographs confirmed the nature of the structural abnormality and clearly demonstrated the anatomic basis of the diffusion defect. The alveolar epithelium formed a continuous layer lining the airspace. However, the large type II cells were more numerous than normal and the type I cells, instead of having...
DISTINCTIVE ULTRASTRUCTURAL FINDINGS IN IDIOPATHIC INTERSTITIAL PNEUMONIA

extremely fine cytoplasmic extensions, were frequently greatly swollen. The alveolar and capillary basement membranes were quite uniform and normal in appearance. The interstitium, which is very scanty in normal lungs, made up the major portion of the increased alveolar septal volume. In addition to the cellular infiltrate, there was considerable interstitial edema. The alveolar capillaries, instead of occupying approximately 50 percent of the area of the septum as in normal lung sections, were difficult to find or absent in most fields. In addition, they were deeply buried within the interstitial exudate and had markedly swollen endothelial cytoplasm. A typical area is shown in Figure 2. Capillaries bulging into the alveolar lumen could be found in only a few sections. The minimum width of the air-blood barrier in the most normal-appearing capillaries found was, however, 1.09 (±0.15) microns, as compared to 0.35 (±0.03) microns in a similarly prepared normal lung. Most of the threefold increase, which should not be considered as necessarily representing the lung as a whole, was due to endothelial swelling. The patient’s diffusion defect may be considered as the net effect of these alterations.

The unique feature of this case is the presence of the sudanophilic bodies described above. With the higher resolution of the electron microscopy, these inclusions could be seen to have a variable structure, showing in

Figure 3. The cytoplasm of an alveolar macrophage is packed with spherical membrane-limited bodies having a radiating morphology. Inset shows one of these bodies at high power (lead citrate stain × 5,330; Inset, × 51,600).

Figure 4. Inclusions with structure varying from a coarsely radial pattern to an amorphous one are seen within two macrophages. The inclusions within a single cell are of similar structure. Inset shows a pavement-like pattern in another inclusion. Portions of two granules of an adjacent mast cell are seen at the right (lead citrate stain × 20,700; inset, × 31,200).

some cells a homogeneous internal form, and in others a coarse or fine radiating morphology (Fig 3,4). Their appearance in any one cell was, however, quite uniform. As many as 100 of these bodies were visible in a single section of one cell, but many macrophages contained fewer. The bodies measured 1.3 micron in maximum diameter, were membrane-bounded, and were densely osmiophilic. In this respect, they differed from the typical osmiophilic lamellated inclusions of the large alveolar cells, many of which were dissolved out during tissue processing, leaving clear vacuoles. There were no internal membranes or other structures to suggest that these bodies are of biologic origin, and photographs taken at high magnification did not show any crystalline material. They appeared to be present only within alveolar macrophages. None was found either free in the airspace or within the pulmonary tissue.

DISCUSSION

As has been pointed out by Liebow,2 little information has been published concerning the ultrastructure of the lung in cases of interstitial pneumonia or fibrosis. Those cases which have been studied have, with some
exceptions, yielded no specific diagnostic information. Such studies have, however, offered clarification of the nature of the alveolar proteinosis; desquamative interstitial pneumonia; Hamman-Rich lung and of the pulmonary lesion of Goodpasture's syndrome. In addition, electron microscopy of respiratory secretions has aided in the diagnosis of viral and mycoplasmal infections. Electron microscopic examination in this laboratory has demonstrated herpes-like viral particles in one case, the apparently unique inclusions seen in the present case, and nonspecific fibrosis and inflammation in the remaining two.

The nature and significance of these inclusions remains obscure. They appear to contain a significant amount of lipid, but do not resemble either the concentrically arranged myelin-like figures of normal pulmonary surfactant, the pathologically increased lipids seen in alveolar proteinosis, mineral oil, which is amorphous and not osmiophilic, or the inclusions seen in previously described storage diseases. Spherical bodies of similar form have been demonstrated in the type I alveolar cells of rats injected with radioactive macroaggregated albumin. A lung scan was not, however, performed in this patient. The size of the inclusions in this case (1.3 micron diameter) is consistent with the possibility of their having been deposited in the alveoli by inhalation, as is their location within alveolar macrophages. Their variable appearance suggests that the material involved is not metabolically inert, and that the typical radiating form may have been produced by metabolic alteration within macrophages. Finally, in view of the tremendous number of these inclusions which were present in this man's lungs, it seems probable that they acted as an irritant in the production of his disease.

ACKNOWLEDGMENTS: This investigation was supported by NIH Training Grant number CM-415 from 7/1/69 to 6/30/70. We are grateful to Dr. Gottlieb C. Friesinger for permission to publish this report on his patient. Dr. John H. Yardley provided invaluable assistance with the electron microscopy.

REFERENCES


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Left Ventricular Pseudoaneurysm* A Rare Complication of Open-Heart Surgery with Unusual Doppler Manifestations

Manoucher Fallah-nejad, M.D., Denis M. Abelson, M.D., and William S. Blakemore, M.D., F.C.C.P.

A patient with postoperative ventricular pseudoaneurysm is reported. The rarity of this complication is discussed. The unusual flow signal in the velocity Doppler cardiogram and its unique significance are emphasized. The surgical management of the aneurysm and the postoperative disappearance of the Doppler finding are presented.

Ventricular aneurysm is a rare complication of cardiac surgery. In 1957, Smith et al reported two cases of postoperative pseudoaneurysm treated successfully by surgery. There are numerous reports in the literature regarding the surgical aspects of true post-traumatic aneurysms, but very few dealing with aneurysms following cardiac surgery. We are reporting a rare case of left ventricular pseudoaneurysm from the site of the left ventricular vent drain, discovered 18 months after open heart surgery for aortic valve replacement and successfully repaired.

CASE REPORT

A 59-year-old whiskey salesman had a sudden attack of pulmonary edema in February, 1968, at which time an aortic

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