Desquamative Interstitial Pneumonia

ARTHUR S. PATCHEFSKY, M.D. AND WILLIS S. HOCH, M.D.

Thomas Jefferson University Hospital, Philadelphia, PA 19107

ABSTRACT

The clinical and pathologic findings of 13 cases of desquamative interstitial pneumonia (DIP) are presented. The disease is characterized by large numbers of intra-alveolar mononuclear cells. Eight cases showed mild degrees of fibrosis at the time of biopsy. Six cases had arthritis or clinical and serologic features suggesting altered immunological activity. Three patients died of progressive pulmonary insufficiency, and one patient has progressive pulmonary disability. The poor outcome of these patients correlated with the presence of fibrosis in the biopsy suggests that DIP may be the early stage of some cases of diffuse interstitial pulmonary fibrosis.

Leibow, Steer and Billingsley in 1965 first described desquamative interstitial pneumonia (DIP), segregating it from the usual chronic interstitial pneumonias or “UIP” because of the relative lack of fibrosis and more favorable response to steroid therapy. Pathologically, the disease was characterized by large numbers of mononuclear cells in the alveolar space without evidence of necrosis or hyaline membranes. A subsequent report by Gaensler et al totalling 12 cases corroborated the initial report. Only one patient in each series died. Thirteen cases of DIP studied at the Thomas Jefferson University Hospital between 1959 and 1969 have been reviewed. Unlike the previous reports, the outcome of this series has not been as favorable. This report will review our experience with this disease.

Pathology

Our material closely conforms with the description of Liebow et al. All 13 cases showed large numbers of intra-alveolar, mononuclear cells and prominence of the alveolar lining cells. These cells had dense eosinophilic cytoplasm, sometimes containing brown finely granular pigment, which characteristically stained with PAS and, in an occasional case, with the Prussian blue reaction. There was no necrosis of the cells nor were fibrin or hyaline membranes demonstrable within the alveoli. The extent of involvement in the sections ranged from about 30 to 95 percent of the surface area. Mitotic activity was found in the intra-alveolar cells as well as in the alveolar lining cells. This was seen in all cases. Occasional multinucleated forms were seen in the alveolar spaces. The alveolar septa showed focal thickening in eight cases. Mild interstitial lymphocytic and plasma cell infiltration was seen in most cases. Lymphoid nodules, some with germinal centers, were present in all but three cases and interstitial smooth muscle hyperplasia was seen in all cases which increased pro-
portionately with the amount of interstitial fibrosis. In several cases, small pulmonary arteries showed medial hyperplasia. Ten cases had eosinophilic viral-like inclusions in the nucleus of the intra-alveolar cells and alveolar lining cells. These were numerous in three cases but were found only after meticulous search in the others. Identical bodies were described in one case of Liebow's original report as well as in one of Gaensler's series suggesting to these authors that viruses were possibly indicated in the etiology of DIP. To test the specificity of this finding, 12 cases with lung diseases of various etiologies were reviewed. Four of the 12 cases showed similar intranuclear bodies, suggesting that these are not specific for DIP and are not necessarily indicative of viral infection.

Clinical Findings

Nine patients were male. The ages ranged from 30 to 74 years with an average age of 50. The duration of symptoms ranged from three months to five years before diagnostic lung biopsy. The predominant symptom in most cases was that of exertional dyspnea. Five patients had cough, most often non-productive but occasionally productive of small amounts of mucoid sputum. No patient had hemoptysis but seven cases had clubbing of the fingers and four showed exertional cyanosis. Two patients were asymptomatic, their disease being manifest by abnormalities of the chest roentgenogram. One patient had a concurrent pontine glioma. Of particular interest was the presence of musculoskeletal complaints in six patients. Three patients also showed abnormal serologic antibodies. One case had antinuclear factor while another had antinuclear factor, positive LE tests and a positive latex flocculation test. Both of these cases had clinical evidence of arthritis. Another case had a weekly positive latex flocculation and had no symptoms of arthritis. One patient had chronic discoid lupus erythematosus 15 years before the onset of pulmonary symptoms.

Environmental Factors

Possible inciting environmental factors were elicited in two patients. One was a fuel oil truck driver exposed to oil fumes for many years. Another was employed as a precision tool grinder exposed to tungsten carbide dust for 15 to 20 years before the onset of pulmonary disease. This case is of particular importance since the report of Coates and Watson showing interstitial fibrosis in 12 patients exposed to tungsten carbide dust for long periods of time.

Roentgenology

As originally described by Leibow et al, DIP showed a characteristic roentgenographic pattern. Most of their cases were characterized by diffuse basilar infiltrates in both lungs radiating from the hilum. None of our cases showed this pattern, all cases having more diffuse involvement. In eight cases, however, the basilar portions of the lower lobes were the most heavily infiltrated. Roentgenographic differentiation from other causes of interstitial fibrosis or collagen disease could not be ascertained.

Case Histories

Two case histories of special interest are presented illustrating an unfavorable course.

Case 1. H.T. (TJUH#282191).

A 61 year-old white male was admitted to the hospital in August 1969. Six months prior to admission, an abnormal chest X-ray was found (figure 1). Shortness of breath on exertion, after climbing three flights of steps, had begun two years previously and had become gradually progressive. There was no chest pain, wheezing, or cyanosis. The patient had smoked 1.5 packs of cigarettes per day for 30 years but stopped smoking 15 years before. He was a business executive and denied exposure to fumes, asbestos or dust. For several years, morning stiffness of the ankles, which cleared with activity, had been present. There was no swelling, tenderness or deformity of the joints. The respiratory rate was 24 per minute. There were bilateral basilar coarse inspiratory rales. Examination of the heart revealed an accentuated pulmonic second sound. There was marked clubbing of the fingers and toes. A liver
 biopsy was performed because of suspected sarcoidosis. This showed dense inflammatory infiltration of the portal tracts with infiltration and partial dissolution of the bile ducts (figure 2). Pulmonary function tests showed a slightly decreased vital capacity (73 percent of predicted). The oxygen saturation was 92.1 percent at rest and decreased to 78.8 percent with exercise. The laboratory data was normal except for a sedimentation rate of 24 mm per hour and white count of 10,300 with 11 percent eosinophils. Serum protein electrophoresis was normal. The latex flocculation test was negative. The patient underwent open lung biopsy. Histologically, the biopsy was consistent with DIP (figures 3 and 4). The patient was discharged one week later taking prednisone, 40 mg a day, which was gradually tapered as an outpatient to 10 mg per day. Shortness of breath became progressively severe despite increased steroid dosage. This gradually progressed and cyanosis at rest developed. The patient died of cardio-respiratory failure in July 1971. Permission for autopsy was denied.

This patient showed gradually progressing symptoms of dyspnea four to five years before biopsy and died less than two years after biopsy and diagnosis despite the administration of steroids. Histologically, interstitial fibrosis was present although most of the biopsy showed the acute "desquamative" pattern. Mild arthritis of the ankles was present, and the unexplained inflammation of the liver was suggestive of more widespread disease. Arthritis and liver disease have been described in both DIP\textsuperscript{2,5,8,12} and idiopathic diffuse pulmonary fibrosis.\textsuperscript{4,6,12,13,14}

Case 4: J.F. (TJUH#275183)

A 54-year-old white male, a fuel oil truck driver for ten years, was admitted in January 1969 for cough and shortness of breath of two years' duration. He had been in good health and able to do vigorous labor until he contracted a "chest cold" in January 1967, with sore throat and nonproductive cough. Cough medicine and antibiotics did not arrest the cough which continued with the insidious progression of dyspnea. In September 1968, he noted the sudden onset of generalized aches and pains, swelling and stiffness of his fingers bilaterally and pain in the right shoulder. Blue discoloration of the fingers was occasionally noted. A latex flocculation test was positive and he was given Solucortef, 40 mg per day, followed by improvement in his joint symptoms, but dyspnea...
Figure 3. Case 1. Lung biopsy showing large numbers of intra-alveolar cells with little change in the alveolar septae. (H & E ×200)

Figure 4. Case 1. Another area of the lung biopsy showing interstitial thickening by fibrous tissue and chronic inflammatory cells. Areas such as these were sparse. (H & E ×200)
remained severe. He was hospitalized for three weeks where three LE cell preparations were positive and an abnormal chest roentgenogram was observed. He was transferred when his condition failed to improve. Moderate dyspnea at rest with finely scattered rales were observed over both bases, posteriorly (figure 5). An accentuated pulmonic heart sound was heard. He demonstrated mild clubbing and cyanosis of the nail beds of the fingers and toes, but no deformity of the joints. A diminished vital capacity (73 percent of normal) and diminished diffusion capacity as measured by the carbon monoxide diffusion test (8 cc per mm of mercury per minute) was recorded. The oxygen saturation at rest was 93 percent. The fluorescent antinuclear antibody test was strongly positive in a 1 to 10 dilution. An open lung biopsy was performed in January 1969 which showed DIP with focal areas of interstitial fibrosis (figures 6 and 7). Post-operatively, the patient was given 70 mg of prednisone a day and was discharged three weeks later. Since discharge, dyspnea and cyanosis have progressed to the point where he is severely incapacitated and cannot work. He has had two subsequent hospital admissions for severe pulmonary insufficiency at another institution. Immunosuppressive drugs were added to his steroid regimen with no improvement.

This patient’s illness began as an apparent upper respiratory tract infection and progressed to severe pulmonary insufficiency despite steroid and immunosuppressive therapy. Symptoms of arthritis followed those of his pulmonary disease and autoantibodies were demonstrated. This suggests a possible underlying “collagen disease” diathesis. The clinical course, results of therapy and associated symptoms do not allow differentiation from idiopathic diffuse pulmonary fibrosis or pulmonary fibrosis associated with collagen diseases.

Treatment and Outcome

Follow-up was obtained in all patients ranging from 2 to 11 years after the onset
of symptoms. One patient died from an intercurrent pontine glioma. Of the remaining 12 cases, three died of progressive pulmonary insufficiency while one continues to show progressive severe dyspnea. Three patients continue to have pulmonary symptoms which are more or less static. One patient died of peritonitis after ruptured diverticulitis of the colon 11 years after the onset of disease. Her disease failed to progress clinically. Three patients have shown clinical improvement. Corticosteroids were used in all but one patient (case 5).

All patients who died or showed progressive pulmonary insufficiency had areas of fibrosis in the biopsy (table I). These areas were not marked and the biopsy still maintained the predominantly "desquamative pattern." One patient who showed improvement had mild fibrosis. It is possible that sampling overlooked similar foci in the other cases, however. These findings suggest that interstitial fibrosis in DIP has an adverse effect on the course of the disease.

In two previous reports, the outlook for DIP was deemed to be quite favorable by virtue of the prolonged clinical course and favorable response to steroids. Our results have not been as favorable. Four patients have died or showed progressive disease. As originally defined, DIP shows little fibrosis. However, even in the original report as well as in subsequent papers fibrosis has been shown to occur together with the desquamative pattern. This raises the question of whether or not DIP represents the early stage of some cases of chronic interstitial fibrosis as first suggested by Scadding and Hinson. The associated musculo-skeletal complaints and abnormal or altered immunological activity in several of our patients as well as in other reports also suggests relationship to idiopathic chronic interstitial fibrosis. The value of separating DIP from this spectrum of diseases lies in the recognition of cases that may be potentially helped by adequate and prompt steroid medication. However, not all cases may respond favorably, although it is possible that sampling error may have
TABLE I
CLINICAL COURSE AND PATHOLOGY OF DESQUAMATIVE INTERSTITIAL PNEUMONIA (DIP)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/Sex</th>
<th>Clinical Findings</th>
<th>Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. S.W.</td>
<td>45/WF</td>
<td>Mild dyspnea. Chronic discoid LE. Pain in knees, shoulders, elbows with morning stiffness.</td>
<td>±</td>
</tr>
<tr>
<td>7. J.E.</td>
<td>42/WM</td>
<td>Dyspnea. Ascariasis.</td>
<td>0</td>
</tr>
<tr>
<td>11. D.L.</td>
<td>51/WM</td>
<td>Dyspnea.</td>
<td>0</td>
</tr>
<tr>
<td>12. M.I.</td>
<td>30/WF</td>
<td>Mild dyspnea. Weekly positive latex flocculation test.</td>
<td>0</td>
</tr>
</tbody>
</table>

overlooked areas of more advanced fibrosis in those of our series who had an unfavorable outcome.

The etiology of DIP as well as the other interstitial pneumonia is obscure. Clinical and ultrastructural studies have failed to reveal evidence of viral causation. That certain environmental factors may be implicated is suggested by the report of Corrin and Price, showing DIP associated with asbestosis as well as the report of Coates and Watson, showing a DIP-like syndrome in tungsten carbide workers. Altered immunological activity may be a factor in the etiology or pathogenesis of this syndrome as suggested by the abnormal serologic antibodies and arthritic symptoms in our cases as well as in other reports. Discovery of the cause of early alveolar injury may lead to the prevention of interstitial fibrosis.

Acknowledgment
Thanks are extended to Miss Lois Greenberg and Miss Theresa Calabro for secretarial assistance.

References


