Desquamative alveolar disease (desquamative interstitial pneumonia): case report¹

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Desquamative interstitial pneumonia is a disease characterized by massive alveolar cell proliferation and desquamation with sparse interstitial involvement. The reported case shows an unusually widespread radiographic reticulo-nodular image and abundant alveolar cells in the sputum. Functional studies reveal the expected diffusion defect with practically normal mechanical properties of the lung, in contrast with interstitial fibrosing lung diseases. On the basis of the pathological findings, especially the behaviour of alveolar cells, the individuality of this disease is discussed. We think that it is different from other diseases classed as varieties of a single disease or as different entities under the names of primary interstitial fibrosis or chronic fibrosing alveolitis.

Liebow (Liebow, Steer, and Billingsley, 1965) separated from the complex group of idiopathic pulmonary interstitial fibrosis a disease which they described as desquamative interstitial pneumonia (DIP). Its principal and distinctive pathological characteristic was a uniform and widespread proliferation of type II or granular cells of the alveolar epithelium which massively desquamated into the alveolus. Interstitial septa were slightly or moderately involved, except in very late stages of the disease.

Gaensler, Goff, and Prowse (1966) described 12 additional cases, and in 1967 Goff, McNary, and Gaensler added another. The present report describes a case of DIP in which the mechanical properties of the lung were studied, and cytology of the sputum revealed the same desquamated cells that were found in the lung biopsy specimen.

CASE REPORT

O. L. B., a 60-year-old man, had since 1964 presented progressive exertional dyspnoea and cough with scanty mucoid sputum. In September 1965 a chest radiograph revealed diffuse bilateral mottling diagnosed as miliary tuberculosis and the condition was treated as such. After three months treatment was discontinued on account of consistently negative bacteriological examinations and persistence of the radiographic findings. Clubbing of the fingers had been

noticed several months prior to the first symptoms. The past history was not contributory, except for prolonged heavy smoking. He worked as a mechanical engineer in a copper mine, but had had no significant exposure to silica.

On physical examination dry fine crepitations were heard over both lung bases, and marked cyanosis, which increased during exercise, was present. Chest radiographs showed some hilar enlargement, and widespread abundant fine reticular and nodular mottling which was concentrated in both lower regions of the lungs with relative indemnity of the costodiaphragmatic angles (Figs 1 and 2).

The blood sedimentation rate was 34 mm./hour and the plasma proteins were 6.8 g./100 ml. with 37% gamma-globulins. Other blood tests were negative, and an electrocardiogram showed only a clock-wise rotation of the heart.

Lung-function studies are summarized in Tables I, II, and III.

With the hypothesis of fibrosing interstitial lung disease a biopsy was taken from the lingular segment of the left upper lobe by a thoracotomy.

Histological examination showed a well-preserved general lung architecture (Fig. 3). The alveolar spaces were filled with desquamated large alveolar cells with an eosinophilic cytoplasm and a round or oval, generally eccentric, nucleus, which was homogeneously chromatinic (Fig. 4). The cytoplasm contained fine brownish-yellow granules which were PAS-positive and did not take up Prussian blue. The cells were either free or formed syncytial masses. Some of the cells were multinucleated (Fig. 5), and a few showed macrophagic activity with inclusion of small fragments of connective or elastic tissue. The same type of cells

¹With the support of the Gildemeister Foundation, Santiago, Chile

lined the alveolar walls and gave them a thickened appearance. In the interstitial space some lymphocytes and reticular cells were observed, with moderate and irregular fibrosis of the argyrophilic reticulum. No alteration of elastic fibres was present and the interstitial reticular structure was preserved, except in the fibrosed areas mentioned.

TABLE I
LUNGS VOLUMES AND MECHANICS

	May 1966	November 1967	Predicted Normal
Vital capacity (l. B.T.P.S.)	3.30	3.51	3.50
Residual volume (l. B.T.P.S.)	1.72	—	1.45
Total lung capacity (l. B.T.P.S.)	5.02	—	5.05
RV/TLC %	32	—	28
Maximal breathing capacity (l./min.)	139	114	93
Forced expiratory volume 1 sec. % C.V.	73	68	80
Lung dynamic compliance (l./cm. H ₂ O)	0.114	—	0.123
Lung specific compliance (l./cm. H ₂ O/F.R.C.)	0.034	—	0.055
Total lung work (kg.m./min.)	2.62	—	1.2
Elastic lung work (kg.m./min.)	2.17	—	0.75
Non-elastic lung work (kg.m./min.)	0.45	—	0.45

The bronchioles were normal and contained abundant desquamated cells. The pulmonary vessels,

especially the arterioles, exhibited moderate muscular thickening with narrowing of the lumen.

Corticosteroids were started but had to be discontinued because of a severe respiratory *Pseudomonas aeruginosa* infection, finally controlled with antibiotics.

TABLE II
ALVEOLAR VENTILATION

	May 1966		November 1967		Predicted
	Rest	Exercise	Rest	Exercise	Rest
VT (ml. B.T.P.S.)	1,080	1,530	725	1,435	500
Respiratory rate per minute	17	36	16.5	26	14
V _E (l. B.T.P.S.)	18.4	55	12	37	7
V _A (l./sq.m.)	4.25	10.3	2.5	7.05	2.5
V _D /V _T %	71	72	67	68	33
Q _R .E. . . .	0.99	0.90	1.0	1.0	0.80

One year later the patient returned in practically the same clinical and functional condition (Tables I, II, and III).

Examination of the centrifuged sputum (Figs 6 and 7) showed abundant alveolar granulocytes and many large multinucleated cells, similar to the elements observed in the histological specimens.

A new course of corticosteroids was tried, using 6 mg. of betamethasone daily. After 20

FIG. 1. Chest radiograph (November 1967) shows reticulo-nodular bilateral mottling and hilar enlargement.

days it was reduced to 2 mg. as a maintenance dose. Three months later dyspnoea was markedly reduced and the patient was able to climb a flight of stairs and walk six blocks. Granular cells in the sputum were less abundant.

FIG. 2. Chest radiograph. Close-up view of the left middle third shows a reticular pattern.

Pao₂ increased from 46 to 56 during rest and from 39 to 49 during exercise, with a reduction of the alveolar-arterial gradient, which was 56 ml. in 1966, to 42.5 mm. Pulmonary dynamic compliance increased from 0.120 to 0.240 l./cm. H₂O.

No radiological changes were observed.

TABLE III
ARTERIAL BLOOD GASES AND DIFFUSION

	May 1966		November 1967		Predicted Value
	Rest	Exercise	Rest	Exercise	Rest
SaO ₂ %	78.5	69.3	78	67	95
PaO ₂ (mm. Hg) ..	101	101	98.5	97	90
PaO ₂ (mm. Hg) ..	48	38	45	38.5	80
A-aO ₂ difference (mm. Hg) ..	53	65	53.5	58.5	> 12
PaCO ₂ (mm. Hg) ..	36	34	39.5	40	40
pH ..	7.37	7.38	7.39	7.38	7.40
DLCO (ml./min./mm. Hg) ..	5.08	9.7	7.7	7.75	19

DISCUSSION

The pathological findings are identical to those described in the previously mentioned papers. The clinical history is also similar, but a difference can be seen in the radiographic picture. Generalized and marked reticulonodular shadows are not

commonly observed in DIP, especially in a patient with a relatively short history and absence of marked fibrosis (Liebow *et al.*, 1965 ; Gaensler *et al.*, 1966).

FIG. 3. Lung biopsy specimen: general aspect of cell-filled alveolar spaces (H. and E. $\times 40$).

Another special feature is the cytological appearance of the sputum smear, which could be a useful diagnostic element when present. It is, though, necessary to perform this examination in a significant number of early cases of other types of fibrosing lung diseases before the finding can be adequately interpreted.

The functional derangement was comparable to what has been described in other patients (Liebow *et al.*, 1965 ; Gaensler *et al.*, 1966 ; Goff *et al.*, 1967). Lung volumes were normal and no signs of obstructive disease were present. A severe resting hypoxaemia with a Pao₂ of 48 mm. Hg was markedly exaggerated during exercise and the alveolar-arterial O₂ gradient was increased to 53 mm. Pao₂ was normal and DLco was restricted to 5.08 ml./min./mm. Hg at rest and 9.7 ml./min./mm. Hg during exercise.

Specific lung compliance was reduced to 0.034 ml./cm. H₂O/l. F.R.C. and the total lung work was moderately elevated on account of an increased elastic work. Spontaneous breathing at

rest was deep and slow with a tidal volume of 1,080 ml. and a frequency of 17/minute. These findings are in contrast with the very low compliance and the fast and shallow breathing pattern of other pulmonary fibrosing diseases (Lisboa and Feretti, 1967; Lourenço, Turino, Davidson, and Fishman, 1965). It is worth while to point out that no detectable functional deterioration was observed after 18 months without treatment.

The individuality of this disease, as suggested by Liebow *et al.* (1965) and supported by Gaensler *et al.* (1966), has been questioned by Scadding and Hinson (1967), who consider it to be an early phase of diffuse fibrosing alveolitis or idiopathic interstitial fibrosis of the lung. This position is based on the observation that typical DIP features can be seen in patients not otherwise different from the rest of the group as a whole. Nevertheless, the other entities usually grouped under the above-mentioned names, such as muscular cirrhosis of the lung, Hamman-Rich disease, etc., have other characteristics which permit their differentiation in the non-terminal stages.

FIG. 4. Lung biopsy specimen: cells within the alveoli, showing an eosinophilic cytoplasm with brownish granules (H. and E. $\times 100$).

Muscular cirrhosis (Rindfleisch, 1898; Jerry and Ritchie, 1964) is a focal disease which becomes widespread by growth and confluence (Rodriguez,

1967), in sharp contrast with the uniformity found in DIP. Elastic fibres are thickened and fragmented and marked smooth muscle hyperplasia is usually present. Unpublished data obtained from successive biopsies in two brothers, 6 and 8 years old, show that desquamation, although present in the early stages, is of only moderate degree and that the desquamated cells have an extraordinarily marked macrophagic activity with early destruction of the alveolar architecture.

FIG. 5. Lung biopsy specimen: slight increase of collagen fibres in alveolar septa. In the left upper quadrant a multinucleated giant cell and a mitotic figure can be seen (Van Gieson $\times 100$).

Hamman-Rich disease shares with DIP the generalized character, but it is not as uniform (Hamman and Rich, 1944; Cross, 1957; Livingstone, Lewis, Reid, and Jefferson, 1964; Rodriguez, 1967). Granulocyte proliferation and desquamation are present, but as a transient and not a prominent feature. Inflammatory cell infiltration and thickening of the interstitial spaces are marked from the beginning.

All these diseases, except acutely fatal Hamman-Rich disease, show a progressive course towards a honeycomb lung, usually in a few years, and the results of corticosteroid treatment have been disappointing (Livingstone *et al.*, 1964;

Cruz, Diaz, Corrales, and Salvestrini, 1967). On the other hand, DIP runs a very prolonged course with late development of fibrosis. Corticosteroids have a good, and sometimes spectacular, effect (Liebow *et al.*, 1965 ; Gaensler *et al.*, 1966).

FIG. 6. Sputum smear shows abundant alveolar cells. A giant multinucleated cell can be seen (H. and E. $\times 40$).

Although on clinical grounds differentiation is usually easy, another disease which has to be considered in the pathological diagnosis is idiopathic pulmonary haemosiderosis. The DIP cytoplasmic brownish granules have been mistaken for haemosiderin (Gaensler *et al.*, 1966), but this substance can be recognized with the specific Prussian blue stain. Histological confusion may also derive from the fact that haemosiderosis presents alveolar cell proliferation and desquamation (Soergel and Sommers, 1962), thus forming with DIP, muscular cirrhosis, Hamman-Rich, alveolar proteinosis, idiopathic pulmonary haemosiderosis, etc., a group of diseases which present as an early, and probably fundamental, element a disorder of the alveolar epithelium.

Earlier and more frequent pulmonary biopsies are needed to increase knowledge in this field. The small risk of the procedure is warranted by its usefulness for selecting appropriate cases for in-

tensive corticosteroid treatment: the presence of marked fibrosis renders the therapy useless and therefore the dangers of its use are not justified.

FIG. 7. Sputum smear. On high magnification cells found in the sputum show the same characteristics as those desquamated into the alveoli (H. and E. $\times 240$).

The pathological characteristics of the disease are only partly described by the use of the term desquamative interstitial pneumonia. The basis of the disease lies in the alveolar epithelium which proliferates and desquamates into the alveolus. Therefore these spaces are not filled with inflammatory cells, as in true pneumonia, and the intra-septal reaction is not as predominant as the term 'interstitial' would suggest. Perhaps desquamative alveolar disease would describe the condition more objectively, besides laying the emphasis on the fundamental alveolar epithelium pathology.

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