Granular Pneumocyte and Pulmonary Fibrosis*

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Electron microscopic study of lung tissue in the state of fibrosis from desquamative interstitial pneumonia, idiopathic hemosiderosis and diffuse interstitial fibrosis of unknown etiology demonstrated the abundant presence of acanthomes in granular pneumocytes which were adjacent to developing elastin fibers or collagen. By analogy with similar observations in fibroblasts, it is suggested that the granular pneumocyte may be important to the process of repair in the lung.

The granular pneumocyte of the lung was first described less than two decades ago. Since then, and at an increasing rate within recent years, electron microscopic studies have provided evidence that these are the cells which proliferate along the surface of the alveolar wall and in some instances shed off into alveolar spaces. This has been shown to occur in man in such diseases as pulmonary alveolar proteinosis, idiopathic pulmonary hemosiderosis, busulphan lung, and desquamative interstitial pneumonia. In animals, it has been observed with oxygen toxicity, crotalaria pulmonary hypertension and ozone exposure. This impressive proliferation of granular pneumocytes under differing circumstances is either followed by resolution or irreversible diffuse interstitial pulmonary fibrosis, although there are relatively few long-term observations in the animal studies. In this report, evidence is presented which would suggest the hypothesis that the granular pneumocyte plays a functional role in the development of pulmonary fibrosis.

Materials and Methods

Six lung specimens were available for electron microscopic study with the following pathologic diagnoses: one biopsy with diffuse pulmonary fibrosis of unknown etiology, four biopsies with desquamative interstitial pneumonia, and one autopsy specimen with idiopathic pulmonary hemosiderosis. Two specimens from normal lung biopsies were studied as a control. Blocks of tissue (1 mm³) were fixed in 3 percent glutaraldehyde, postfixed in 1 percent osmium tetroxide and embedded in Epon (812). Sections were stained with uranyl acetate and lead citrate and examined in a RCA EMU-4B electron microscope.

Results

Clinically and histologically all specimens were already in a stage of obvious fibrosis but still had an abundant proliferation of cellular components. In electron micrographs, the conspicuous proliferation

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Figure 1. Idiopathic pulmonary hemosiderosis. Proliferated granular pneumocytes (A) along the surface of alveolar wall with adjacent developing collagen fibrils (B). (x 8,800)
Idiopathic pulmonary hemosiderosis. A granular pneumocyte (A) lying immediately adjacent to elastic fibers (B). (× 8,800)

of granular pneumocytes along the alveolar wall was characteristic in all sections, together with formation of collagen tissue within the alveolar walls (Fig 1). It was a prominent finding that the proliferated granular pneumocytes were lying adjacent to the developing elastin fibers or collagen (Fig 2). Utilizing a higher resolution over the area where granular pneumocytes are in the immediate vicinity of elastin or collagen, a search was made for any evidence that the granular pneumocytes could be concerned with the production of fibrosis. W. H. Fahrenbach and associates, reported on acanthosomes (spiny vesicles) found in fibroblasts up to 2300 Å in diameter as they approach the surface of the cells, which have been interpreted as a mechanism of secretion of protein polysaccharide components of connective tissue. Goldberg and Green also mentioned a mecrocrine type of secretion of collagen by vesicular elements. On our sections, electron microscopy demonstrated many acanthosomes in the granular pneumocytes near the surface of these cells adjacent to the extracellular accumulation of elastin fibers or collagen (Fig 3-6). They were always spherical in shape, measuring about 1700 Å in diameter, with clear centers. The membranes which surround these vesicles were not distinctly demonstrated with the stains used, but they were bordered by the rather thick condensed layer of flocculent material. The shape and other characteristics of these vesicles were structurally identical with those previously described. The acanthosomes which we observed in areas of fibro-
sis were definitely more conspicuous in numbers than they were in other locations not associated with collagen formation.

Although the granular pneumocyte is the principal cell which proliferates in a variety of lung diseases, the stimulus for this proliferation and the possible functions served by the cell remain unknown. Since fibrosis is often associated with the increased numbers of granular pneumocytes, it seems possible that they may play a role in fibrogenesis.

Acanthosomes have been found in various tissues and interpreted functionally as being associated with protein transport, although the region of their origin has not been established. The interpretation that fibroblasts produce their essential components of collagen extracellularly by way of acanthosomes is still within the realm of speculation. It might also be premature to conclude that the presence of acanthosomes in the granular pneumocyte demonstrates the ability of this cell to produce fibrosis. But the same findings in granular pneumocytes as observed in fibroblasts regarding the postulated site of fibrillogenesis certainly suggests this may be an important function of this cell. Investigation of this possibility would certainly seem warranted and could be accomplished in an experimental animal. Proliferation of granular pneumocytes can be induced by exposure to oxygen in high concentrations, carbon dioxide and ozone, etc so that periodic observations may be made for evidence of fibrillogenesis in these cells.

REFERENCES

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