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Brief Note

Immunohistochemical Study of Epithelial Membrane Antigen in Inflammatory Lung Diseases

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Key words : EMA — immunohistochemistry — alveolar epithelium — inflammatory lung disease — pulmonary fibrosis

Pulmonary fibrosis is the end-stage condition for a variety of lung diseases in which the original cause of injury may not be determined with certainty.[1,2] There are, however, some architectural patterns which may reflect similarities in their disease process and/or tissue response. We presume four types of fibrosing processes in lung tissue; namely, (i) intra-alveolar organization (budding), (ii) intra-alveolar obliteration, (iii) incorporation, and (iv) interstitial fibrosis. For the establishment of the last three fibrosing processes, we postulate that diffuse loss of alveolar epithelia is a prerequisite. In intra-alveolar organization, which can be seen in chronic infective pneumonias (organizing pneumonias), the alveolar epithelia are well preserved for the most part, and the organization of an intra-alveolar fibrinous exudate takes place through the areas of focally damaged alveolar epithelium and its basement membrane.[3] When these structures are entirely preserved, the mechanism of intra-alveolar organization does not occur. In order to determine whether our hypothesis was correct or not, it was necessary to observe alveolar epithelia in large areas of lung tissue and in all stages of bronchopneumonias. Electron microscopic study limits the area of examination, but, as reported in a previous communication,[4] epithelial membrane antigen (EMA)[5] provides a good tool for identifying alveolar epithelia at the light microscopic level. Therefore, we immunohistochemically stained lung tissue sections of bronchopneumonia from the early through unresolved stages; that is, organizing pneumonia, with antisera against EMA.

Lung tissues utilized for this study were obtained from four autopsy cases with bronchopneumonia in various stages. Lungs were fixed by infusion of 10% buffered formalin through the airway, and tissue blocks were taken, processed routinely and embedded in paraffin. After deparaffinization, 4 μm thick sections were stained immunohistochemically with mouse antihuman EMA (Dako, Santa Barbara, California) as described in our previous communication.[4]

The histological changes in the bronchopneumonia we examined were as follows. During the early stage a few scattered neutrophils were observed in the alveolar spaces (Fig. 1). In a case of severe bronchopneumonia, the alveolar spaces were filled with a large number of neutrophils with some fibrinous materials and there were areas with and without type II pneumocytic hyperplasia (Fig. 2). In the early stage of intra-alveolar organization, fibrous tissue plugs (Masson bodies) were found in the spaces (Figs. 3,4). In addition, there was a case of so-called interstitial neutrophilic pneumonia, which most likely represents septic pneumonia. In that case, the alveolar walls were found to have been infiltrated

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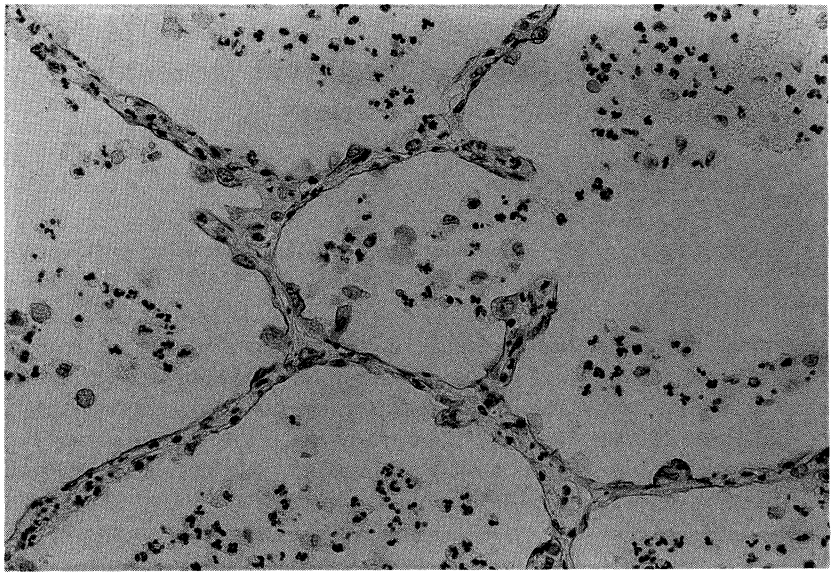

Fig. 1. Early stage of bronchopneumonia. Alveolar epithelia show positive staining for EMA. Note that type II pneumocytes are occasionally hyperplastic. (Immunoperoxidase-hematoxylin for EMA, ×250)

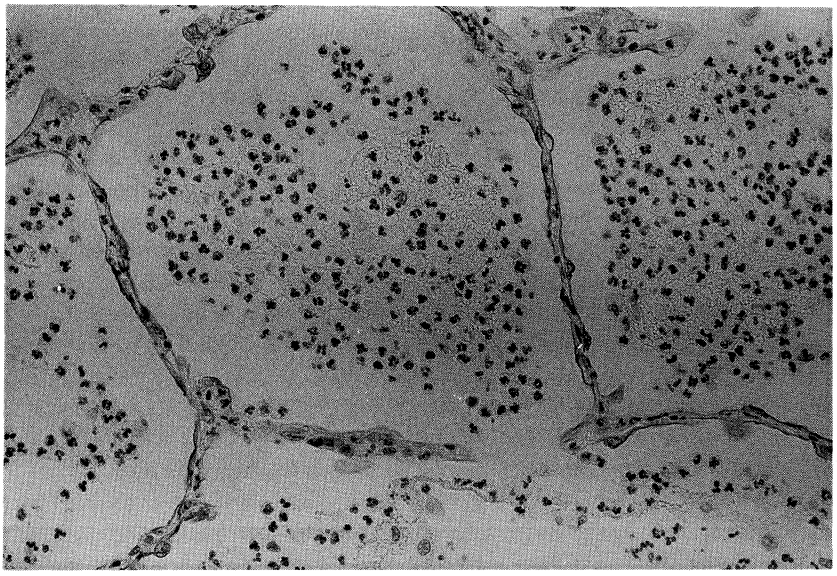

Fig. 2. Severe bronchopneumonia. Alveolar lumens are filled with numerous neutrophils. Most alveolar epithelial cells retain positive staining. Some, however, are immunonegative in areas. (Immunoperoxidase-hematoxylin for EMA, ×200)

by neutrophils (Fig. 5). In all areas of pneumonia, alveolar epithelia showed strong immunoreactivity for EMA. However, in severe pneumonia cases as well as interstitial neutrophilic pneumonia cases, small areas of immunonegative alveolar lining have occasionally been observed. This may have been the result of false

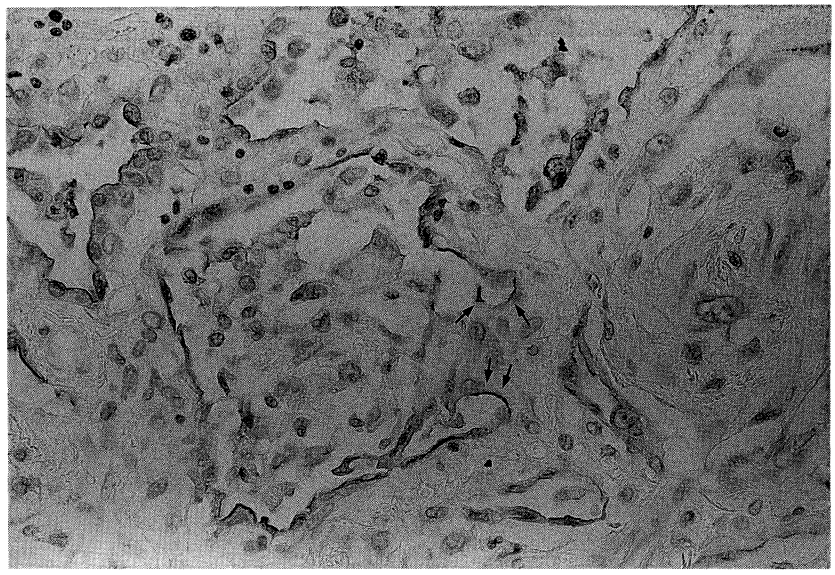

Fig. 3. Early stage of intra-alveolar organization (Masson bodies). The alveolar walls are lined with immunoreactive epithelial cells. Regenerative epithelial cells cover the surface of the fibrous tissue plug near the stalk. They are strongly immunoreactive (arrows). (Immunoperoxidase-hematoxylin for EMA, ×300)

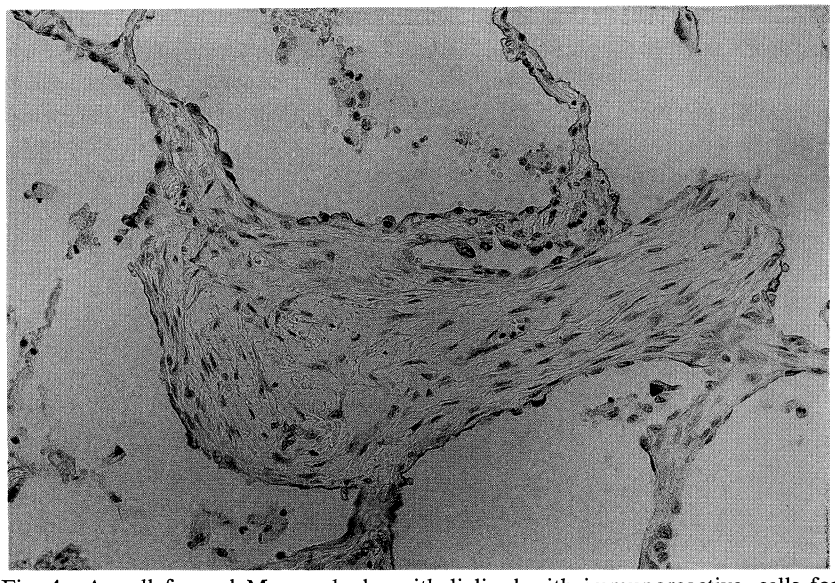

Fig. 4. A well-formed Masson body epithelialized with immunoreactive cells for the most part. (Immunoperoxidase-hematoxylin for EMA, ×200)

negative staining or invisibly weak staining. If such areas are truly negative, it may be considered that they provide the sites for intra-alveolar organization. Even in the case of organizing pneumonia in this study, the alveolar walls were covered with an immunoreactive epithelial lining. Masson bodies were occasion-

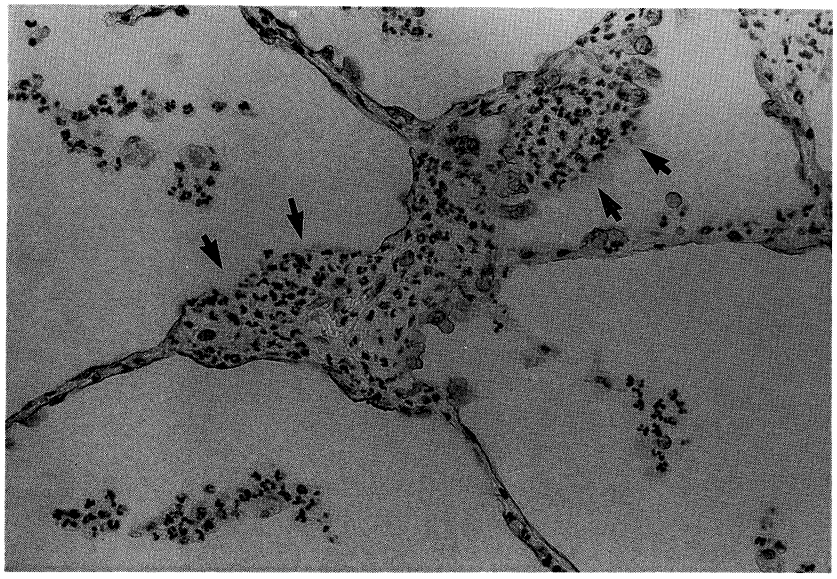

Fig. 5. Alveolar walls with infiltrating neutrophils in the interstitium. Alveolar lining is focally immunonegative (arrows). (Immunoperoxidase-hematoxylin for EMA, ×250)

ally and partially covered with possibly regenerative EMA-immunoreactive plump epithelia, which were usually present near the stalk of organization.

From these findings, we consider that alveolar epithelium remains intact for the most part throughout the stages of inflammation caused by bacterial infection, and that remaining epithelia as well as regenerative epithelia possess immunoreactivity for EMA. Therefore, EMA immunohistochemistry should be useful for identifying epithelial lining even in other types of fibrosing lung diseases. In addition, the results of this study in part support our view about the process of intra-alveolar organization.

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