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Intraluminal Polypoid Fibrosis of the Lung

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ABSTRACT. The present communication describes the morphology and pathogenesis of intraluminal (or intra-alveolar) polypoid fibrosis of the lungs, which is a condition characterized histologically by the presence of polypoid fibrous tissue masses protruding into and filling lumens of the airways or airspaces. Intraluminal polypoid fibrosis is further subclassified into three types. The first type probably represents a primary injury of respiratory bronchioles and alveolar duct walls which directly leads to polypoid fibrous tissue formation. This fibrous tissue is generally uniform in appearance and lacks a fibrinous component. The second type results from fibrous replacement of preceding fibrinous inflammation in the airspaces, such as lobular (broncho-) and lobar pneumonia. It is histologically characterized by an admixture of fibrin and fibrous components. The third type superimposes on hyaline membrane formation. The spaces surrounded by the hyaline membrane along the alveolar duct walls are filled with loose fibrous tissue. In all three types, the process of organization originates in the alveolar duct walls, especially at the edge of alveolar mouths. Therefore, we propose the term of "fibrosing alveolar ductitis syndrome" for such disease entities as BOOP, BIP, and organized DAD, in which damage of the alveolar duct wall results in fibrosis.

Key words : lung — fibrosis — intraluminal — Masson body

Pulmonary fibrosis is the end-stage of tissue injury in the lungs. It is usually non-specific and determination of its original cause may be difficult.[1] We have divided the morphology of pulmonary fibrosis into five patterns, which were described in detail in a previous communication,[2] and stressed that identification of such morphological patterns in any pulmonary fibrosis is helpful in speculating on the pathogenesis and/or etiology of the condition. These patterns are interstitial fibrosis, intraluminal polypoid fibrosis, intraluminal diffuse fibrosis of complete type, intraluminal diffuse fibrosis of incomplete type, and hyaline membrane incorporation. Herein, we present more detailed information on intraluminal polypoid fibrosis of the lungs.

DEFINITION OF INTRALUMINAL POLYPOID FIBROSIS

Intraluminal polypoid fibrosis of the lung is a term that denotes conditions that are histologically characterized by the presence of polypoid fibrous tissue masses protruding into and filling the lumens of airways or airspaces (Fig. 1). Although this fibrotic tissue may exist at any level of the bronchioles, alveolar

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ducts or alveolar spaces, in the present communication, we limit our descriptions only to those seen in respiratory bronchioles, alveolar ducts and alveolar spaces. In the early stages of intraluminal polypoid fibrosis, the polypoid tissues are non-epithelialized over the luminal surface, which is separated from the original frameworks of the alveolar duct or alveolar walls by remaining slender airspaces

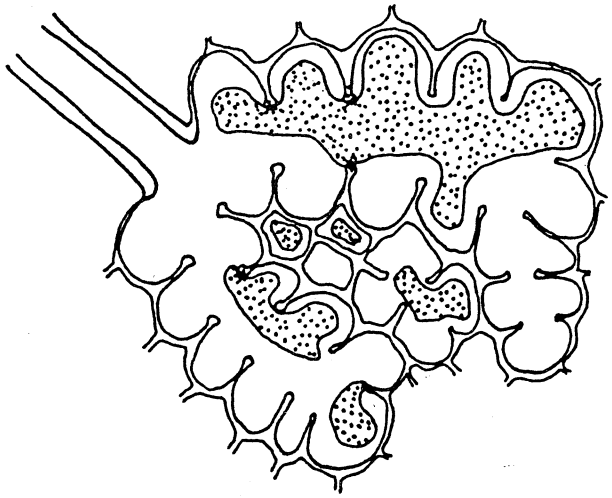

Fig. 1. Schematic diagram of intraluminal polypoid fibrosis.

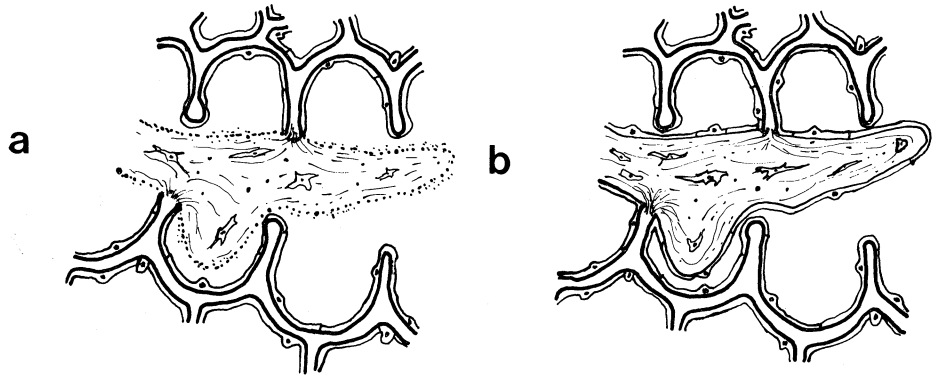

Fig. 2. The diagram shows the surface of intraluminal polypoid fibrosis. The polypoid tissue is not epithelialized in its early stage of formation (a), while it is covered by flat to plump cuboidal epithelial cells in its late stage (b). There is a space or slit between the original framework of alveolar duct wall or alveolar wall and the newly formed polypoid tissue.

(Fig. 2-a). In later stages, they are lined with regenerative flat to plump cuboidal cells which have supposedly migrated from the adjacent walls (Fig. 2-b). This type of fibrosis may be observed in a variety of conditions, such as organizing pneumonia, bronchiolitis obliterans, bronchiolitis obliterans and organizing pneumonia (BOOP), hypersensitivity pneumonitis (extrinsic allergic alveolitis), drug-induced pneumonitis, pneumoconioses, collagen vascular diseases, and idiopathic pulmonary fibrosis.[3] As to its etiology, the morphology of intraluminal polypoid fibrosis is heterogeneous.

VARIETIES OF INTRALUMINAL POLYPOID FIBROSIS

We examined lung tissues from 941 autopsies performed in the Department of Pathology of the Kawasaki Medical School Hospital between the beginning of 1983 and the end of 1987, and found that morphologically different types of intraluminal polypoid fibrosis existed. These were roughly subclassified into three types (Fig. 3). As depicted in Fig. 3-a, the first type of polypoid fibrosis appeared to have arisen from either bronchiolar or alveolar walls as a fibrous mass from the beginning. There were two variants of this type; i.e. fibrous and edematous variants. In the former, the polypoid tissue was entirely composed of fibrous connective tissue (Fig. 4), while in the latter it consisted of edematous stroma with some fibroblasts and scanty collagens (Fig. 5). Characteristically, in the first type, polypoid fibrosis was rather uniform in appearance and did not show any admixture of fibrin exudates. The second type of polypoid fibrosis (Fig. 3-b) seems to develop from preceding fibrinous

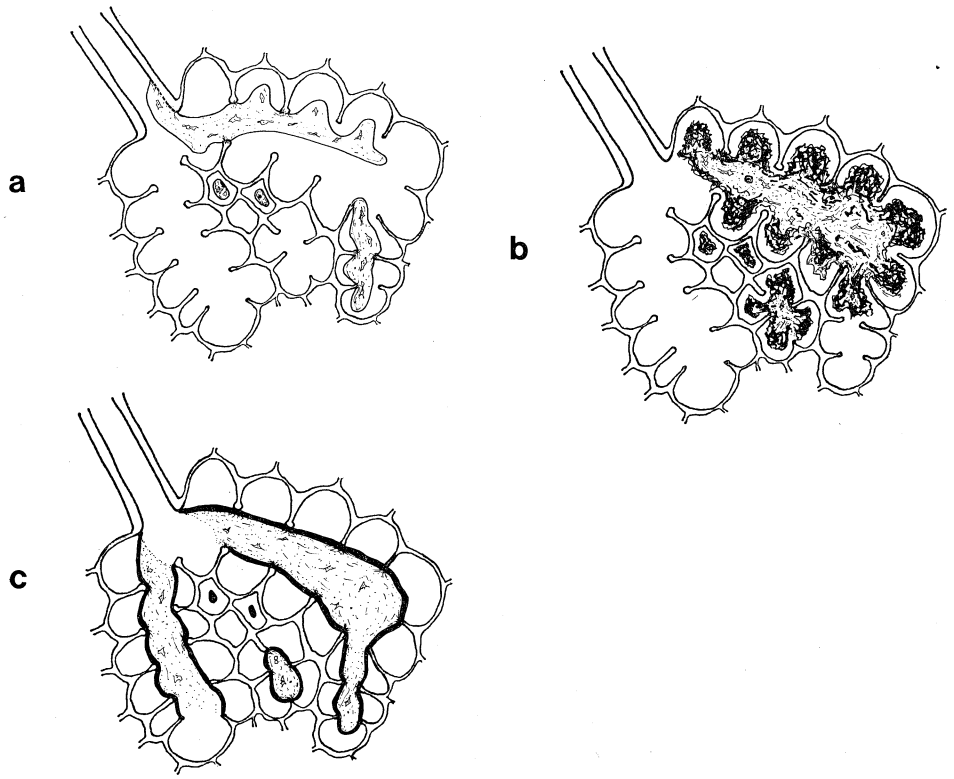

Fig. 3. Schematic diagram of three types of intraluminal polypoid fibrosis.
a. The fibrous tissue in this type is rather homogeneous and is composed of either fibrous connective tissue or edematous stroma with some fibroblasts and scanty collagens.
b. The fibrous tissue in this type is composed of a mixture of fibrin materials and fibrous tissue. The latter component usually penetrates through the center of fibrin masses. This type of fibrosis results from the fibrous replacement of preceding pneumonia.
c. The fibrous tissue in this type is composed of hyaline membrane surrounding edematous fibrous tissue.

pneumonia, probably by the mechanism of organization of fibrin exudates. Therefore, polypoid fibrous tissue usually contained various amounts of fibrin exudate either in the center or along the periphery of exudative masses (Fig. 6). Permeating fibroblasts and macrophages therein were still clearly discernible. The third variant (Fig. 3-c) occurred over the hyaline membrane and filled alveolar ducts almost completely. The central fibrous area was usually loosely fibrous or edematous, and merged into the hyaline membrane at periphery (Fig. 7).

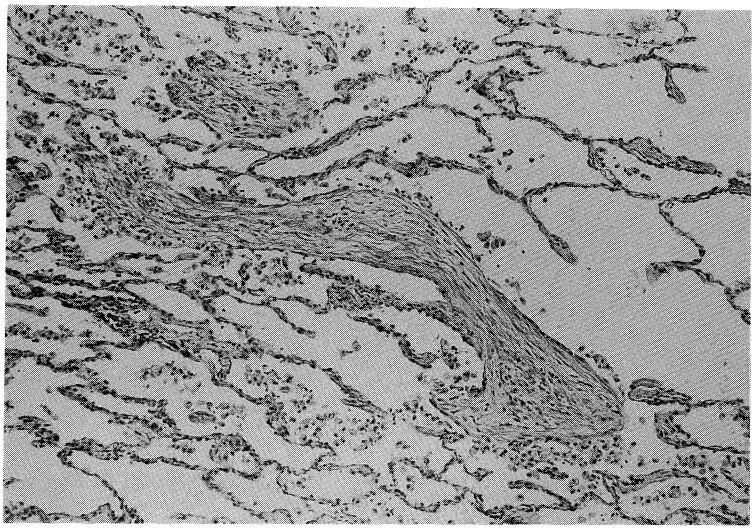

Fig. 4. Intraluminal polypoid fibrosis with homogeneous fibrous connective tissue.

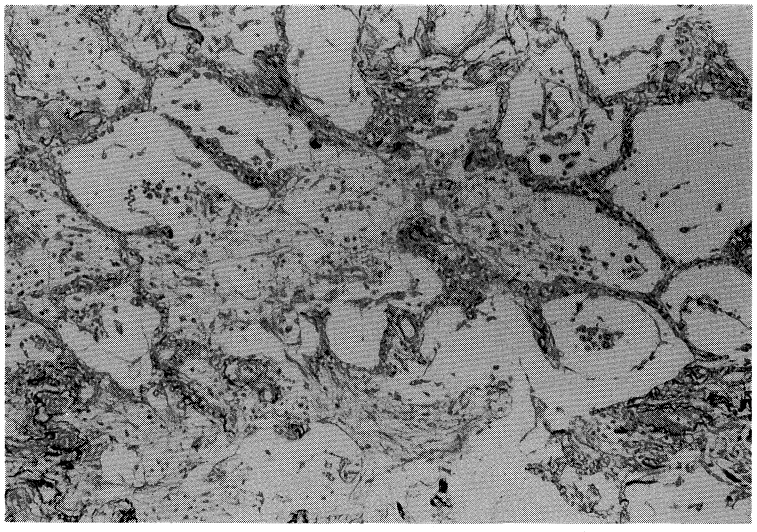

Fig. 5. Intraluminal polypoid fibrosis with edematous stroma. (Elastica van Gieson stain)

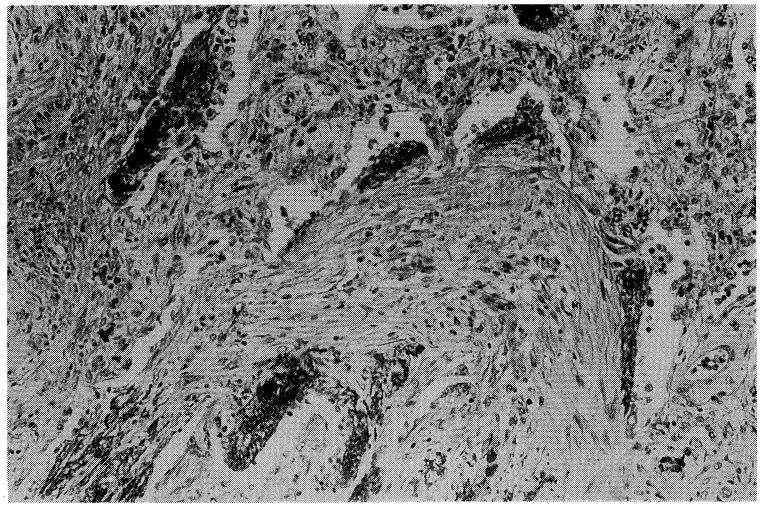

Fig. 6. Polypoid fibrosis composed of a mixture of fibrin and fibrous connective tissue. (Masson trichrome stain)

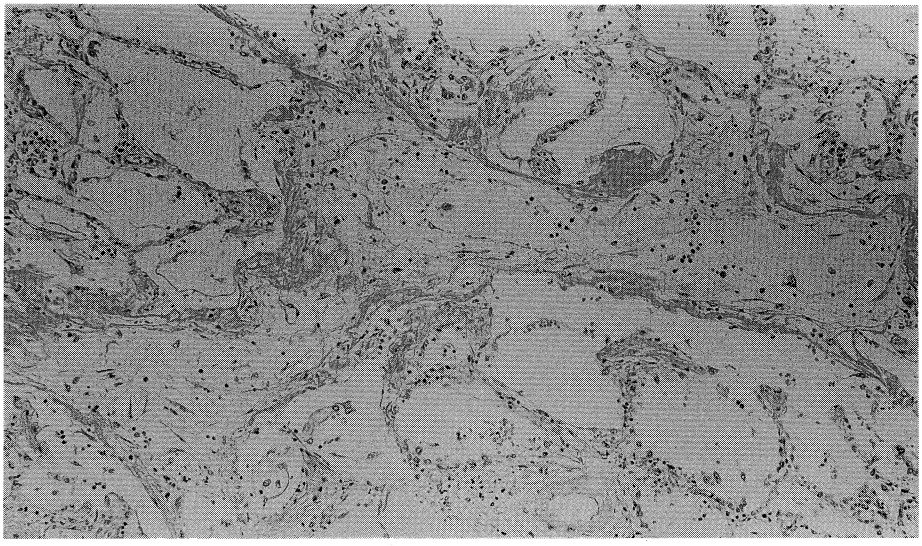

Fig. 7. Intraluminal polypoid fibrosis occurring over the hyaline membrane. The central fibrotic area is usually loosely fibrous or edematous and merges into the hyaline membrane at the periphery.

POSSIBLE PATHOGENESIS OF INTRALUMINAL POLYPOID FIBROSIS

The etiology of intraluminal polypoid fibrosis is variable and mostly unknown. Such a formation of fibrous tissue within airspaces is considered as a non-specific reaction pattern of the tissue to an injury to the airway walls. The variations in the morphological appearance of this fibrosis, however, may reflect a difference in its etiology, although we do not know what causes such a difference. We consider that the first type of polypoid fibrosis results from a primary insult to the airway walls. Necrosis or damage of these walls probably

does not induce a severe acute inflammatory reaction but instead provokes a rapid fibroblastic proliferation. After a short period of weak acute reaction, therefore, granulation tissues grow outward to occlude the lumen. The usual site of granulation formation is the walls of the respiratory bronchioles and alveolar ducts. The alveolar walls are spared. In this sense, it is a fibrosing process involving only small airways, and may be referred to as fibrosing alveolar ductitis. This type of fibrosis occurs in bronchiolitis obliterans, BOOP, hypersensitivity pneumonitis, and drug-induced pneumonitis.

The second type of polypoid fibrosis develops in persisting fibrinous pneumonia. Fibrinous exudate in the airspaces seems to be replaced by granulation tissue originating from the walls of respiratory bronchioles and/or alveolar duct walls. Organization of the exudate in this type is characterized by a mixture of loose fibrous tissue and fibrinous materials. Fibrous tissues usually expand in the center or along the surface of the fibrin mass. This type of fibrosis is exemplified by so-called organizing pneumonia, which occurs after lobar pneumonia or bronchopneumonia.

The third type of polypoid fibrosis apparently occurs after hyaline membrane formation, which appears to be the result of mild to moderate diffuse alveolar damage (DAD). It should be noted that mild to moderate degrees of DAD involve only the alveolar duct walls[4] and, therefore, that mild DAD is another form of alveolar ductitis. On occasion, the hyaline membrane formed after acute alveolar duct injury is associated with edematous exudation in the space surrounded by the hyaline membrane; that is, alveolar duct lumen. Edematous fluid in this location is soon replaced by loose fibrous tissue (edema fibrosis). The histological appearance of this fibrosis type superficially resembles that of the second type. However, they are separable from each other and their pathogenesis and etiology probably differ. This type of fibrosis may be seen in cases of adult respiratory distress syndrome (ARDS), shock lungs, paraquat lungs, burns and other diseases which cause DAD.

INTRALUMINAL POLYPOID FIBROSIS IN LUNG INJURIES SUCH AS BOOP, BIP, AND DAD

Bronchiolitis obliterans and organizing pneumonia (BOOP), a descriptive diagnostic term, was first coined by Epler *et al.*[5] in 1983. It is a spectrum of bronchiolitis obliterans in which polypoid fibrous masses extend down to the alveolar duct and alveolar spaces. Bronchiolitis obliterans and diffuse alveolar damage or bronchiolitis obliterans and interstitial pneumonia (BIP) is a disease entity defined by Liebow and Carrington[6] in 1969. This disease was originally categorized as an interstitial pneumonia, but the processes in the disease are in fact intraluminal and it probably represents a form of BOOP in which the degree of interstitial fibrosis is negligible. In any case, these two disease processes ; namely, BIP and BOOP are characterized by the presence of intraluminal polypoid fibrosis of the first type.

The concept of DAD was established by Katzenstein *et al.*[7,8] It is a descriptive term for a non-specific pathologic sequence of events following acute lung injury and is histologically characterized by prominent hyaline membrane formation. Previously, we have reported on the fate of the hyaline membrane in DAD cases[4] and have shown that some DAD cases result in pulmonary

fibrosis with a characteristic honeycomb appearance. These have been truly designated as organized DAD. In contrast, in some of early DAD cases, the hyaline membranes remain along the alveolar duct wall, and the spaces surrounded by the hyaline membrane are further filled with edematous fluid and may be replaced by loose fibrous tissue in time.

UNIFYING THEORY: A PROPOSAL OF ALVEOLAR DUCTITIS SYNDROME

Formation of the hyaline membrane, which is present mainly along the alveolar duct walls and occludes the alveolar mouth, begins in the walls of the alveolar duct. We tend to consider that this form of lung injury represents an acute inflammatory change of the alveolar duct, and therefore it may be designated as acute or fibrinous alveolar ductitis. Hyaline membranes may be gradually replaced by fibrous tissue, and that fibrous tissue again enters through alveolar duct walls. Its end-stage condition, an organized DAD, is actually organized or fibrosed alveolar ductitis.

In all cases of intraluminal polypoid fibrosis, whether or not the condition develops primarily, organization seems to start from the walls of the alveolar duct and respiratory bronchioles. The edge of Kohn's pore may be an exception and could be another starting point of organization. Intraluminal polypoid fibrosis developing de novo, like that seen in BOOP, also represents a form of alveolar ductitis, since the alveolar duct wall is the site of injury, and we named it "fibrosing alveolar ductitis." The third type of polypoid fibrosis, in which the organizing process involves the replacement of edematous exudate surrounded by the hyaline membrane, may be regarded as secondary alveolar ductitis.

There seem to be disease processes which primarily damage alveolar duct walls rather diffusely. For such primary alveolar duct injuries, we would like to propose the term "alveolar ductitis syndrome." It constitutes a histological spectrum varying from an early fibrinous stage to a late fibrosing stage. Alveolar ductitis may resolve during the early stages in most cases. The late fibrosing stage may be further classified into three forms ; a hyaline membrane incorporation type, an intraluminal polypoid type and a mixed type. They are rather progressive and result in diffuse pulmonary fibrosis. BOOP, BIP and organized DAD are all included in this category and any of these terms may be applied depending on which fibrosing process is most prominent.

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