Alveolar Walls in Mitral Stenosis

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Pathologic alterations of alveolar walls in 95 autopsied patients with mitral stenosis were not frequent. The most frequently encountered change was capillary dilatation, and in 83 per cent of the patients, even this change was slight or absent. Other alterations were focal and involved only small proportions of the area of tissue examined. A generalized increase in the thickness of basement membranes could not be demonstrated.

PATHOLOGIC changes in the pulmonary alveolar walls of patients with mitral stenosis have been described by many investigators. Among the changes described are fibrous thickening, capillary distention, thickening of the capillary basement membranes, and cuboidalization of the alveolar lining cells. It has been pointed out that such pathologic alterations, if widespread, could produce marked physiologic disturbances. However, our own observations on current autopsies of individual patients with mitral stenosis led us to suspect that advanced pathologic changes in the alveolar walls were almost always focal, rather than widespread. These observations stimulate us to review sections of the lungs from a large number of autopsied patients with mitral stenosis. The purpose of this study is to establish the extent and character of abnormalities of alveolar walls in 95 adult patients who died with mitral stenosis.

MATERIAL AND METHODS

Autopsy records and microsections were examined from 95 patients with mitral stenosis as a principal anatomic diagnosis. These patients represent a consecutive series of all such patients over 20 years of age, autopsied at Washington University during the period 1938 to 1954, from whom suitable material was available for study.

Patients were chosen for inclusion in the study on the basis of objective anatomic findings. The average age of the patients was 47 years. A review of the clinical and autopsy records revealed that in 90 of the 95 patients mitral stenosis was the principal abnormality present and the only apparent underlying cause of death. Congestive heart failure was extremely common among the patients, but exact figures of its incidence and duration were difficult to obtain because some of the patients entered the hospital in a terminal state, unable to give an adequate history, and often the records simply stated that the patients had been “in failure for years.” At least 84 of the 95 patients had been in congestive heart failure at some time, 53 for a year or more, and 25 for 3 years or more.

The paraffin blocks of tissue from the lungs of these patients were recut and stained with aldehyde-fuchsin-van Gieson-iron hematoxylin, in order to better demonstrate fibrous and elastic tissue. Sections of lung were also stained with hematoxylin and eosin and in many instances with periodic acid-Schiff and Heidenhain’s stains in order to define more clearly the various components of alveolar walls. All of these stains are as described by Lillie, except for minor modifications. The microsections were examined and various features were recorded including capillary dilatation, fibrosis of the alveolar walls, thickening of capillary basement membranes, and cuboidalization of alveolar lining cells.

Comparative control material was obtained from 106 adult patients who died with a clinical diagnosis of “hypertension” and who had a principal anatomic diagnosis of arteriolar nephrosclerosis (hypertensive group) and from 50 adult patients without chronic pulmonary or cardiovascular disease (normal control group). The sections of lung stained with hematoxylin and eosin from these patients were examined and the extent and degree of capillary dilatation were recorded.

RESULTS

Generalized fibrous thickening of pulmonary alveolar walls was not seen in any patient in this series. Focal areas of lung in which the alveolar walls contained increased amounts of fibrous tissue were present in 9 per cent of pa-
Fig. 1. Twenty-eight-year-old woman with mitral stenosis. Large air spaces lined by cuboidal epithelium and separated by thick walls of connective tissue. The air spaces contain numerous macrophages, filled with hemosiderin. The thick walls are composed of relatively avascular fibrous tissue. Relatively normal pulmonary parenchyma was seen nearby. Aldehyde fuchsin-van Gieson-iron hematoxylin stain, $\times$ 130.

Fig. 2. Thirty-seven-year-old man with mitral stenosis. Normal, slightly collapsed, pulmonary air spaces and alveolar walls. Most of the alveolar walls of the patients with mitral stenosis were not altered. Heidenhain stain, $\times$ 270.

Fig. 3. Twenty-eight-year-old woman with mitral stenosis. Advanced capillary distention in alveolar walls. Hematoxylin and eosin stain, $\times$ 300.

Fig. 4. Same patient as figure 2. An atrial sphincter muscle cut longitudinally. This can be mistaken on hematoxylin and eosin stained sections for fibrosis of alveolar walls if the anatomic relationships of peripheral air spaces are not considered. Aldehyde fuchsin-van Gieson-iron hematoxylin stain, $\times$ 360.

Patients with mitral stenosis, but in extent never exceeded 10 per cent of the area of tissue examined. These focal areas were often associated with intra-alveolar accumulations of hemosiderin-filled macrophages, and were demonstrated most clearly with the Heidenhain and van Gieson stains (figs. 1, 4). Occasionally organized thrombi were seen in small pulmonary arteries adjacent to areas of fibrosis.

Cuboidal epithelium frequently lined the alveoli in the focal areas of fibrous thickening, but this change was never isolated and never
involved more than 10 per cent of the pulmonary parenchyma examined.

Thickening of the “alveolar” and capillary basement membranes was also confined to the areas of focal fibrosis of alveolar walls. Periodic acid-Schiff stains failed to reveal a generalized change in the thickness or character of these basement membranes (fig. 2).

Capillary dilatation was the most common change noted in the alveolar walls (fig. 3), but it was slight in most patients. Moderate or advanced capillary dilatation was observed in 17 per cent of the patients with mitral stenosis, in 15 per cent of the patients in the hypertensive group, and in 4 per cent of the patients in the normal control group. In none of the patients of any group did the dilated capillaries appear to encroach appreciably on the alveolar air spaces.

**DISCUSSION**

Morphologic alterations (other than capillary congestion) in the alveolar walls of 95 patients with mitral stenosis were found to involve only small portions of the pulmonary parenchyma. Fibrous thickening of alveolar walls, thickening of capillary basement membranes, and cuboidal cells lining the alveoli have been described by many observers in the lungs of patients with mitral stenosis.² ³ ⁴ We were able to demonstrate these features in some of our patients. However, most of our patients did not show such changes and in the few that were affected these features were focal. It seems unlikely that alterations of the alveolar walls involved enough of the lungs to be of physiologic significance.

Pulmonary capillary distention was prominent in some of our patients, but the lack of constancy of this capillary distention in association with mitral stenosis, as well as its occurrence in other diseases, indicates that it is not a special feature of mitral stenosis. Pulmonary capillary distention could be related to increased pulmonary venous pressure from any cause, and perhaps to other physiologic disturbances occurring in the agonal state.

Goodale and his associates recently studied biopsies of lung from patients with mitral stenosis, taken at the time of mitral valvulotomy, and found that the increased resistance to pulmonary blood flow in patients with mitral stenosis did not correlate significantly with alterations in the structure of alveolar walls.² This observation is consistent with our conclusion that changes in alveolar walls are in general not sufficiently widespread and severe to be of physiologic importance.

The results of our study indicate that the advanced pulmonary parenchymal changes illustrated herein and described by others² ³ are generally focal and not truly representative of the entire lungs of patients with mitral stenosis.

**Pathogenesis of the Focal Fibrosis of Alveolar Walls.** Even if the physiologic importance of the focal fibrous thickening and cuboidal epithelization of alveolar walls in patients with mitral stenosis is denied, their pathogenesis remains of great interest and warrants discussion, and the presentation of additional, related observations.

Occasionally, an organized, recanalized thrombus is seen in a small pulmonary artery adjacent to a focal area with thickened, fibrous, alveolar walls, suggesting that this thickening may be the result of incomplete infarction of the lung with organization of exudate adherent to the alveolar wall. Intra-alveolar fibrous bodies representing organized exudate are sometimes present and offer some support to this hypothesis. Other support is offered by the similarity of these focal areas of fibrosis in alveolar walls to the pathologic changes in the pulmonary parenchyma surrounding a healed or healing infarct.

Focal accumulations of hemosiderin-filled macrophages are often present in the alveoli that have thickened, fibrous, walls, and this fibrosis may be a reaction to the iron pigment.

Another possible explanation for the formation of these focal lesions of alveolar walls is the organization of material that exuded from the capillaries into the interstitial space of the alveolar walls. This interstitial space, easily demonstrable by electron microscopy,⁶ is so narrow that it cannot be seen in normal lungs with light microscopy but, with the exudation of edema fluid and fibrin, it could be expanded and organization of this exudate could occur. Parker and Weiss¹ described “pericapillary edema” of the alveolar walls in patients with
mitral stenosis, which presumably represents an expansion of the narrow interstitial space of alveolar walls by the exudation of fluid constituents of the blood. We have noted this "pericapillary edema" only rarely and even in these instances, only in occasional, short segments of alveolar walls. However, the possible frequent occurrence of lesser degrees of chronic interstitial edema, not readily demonstrable by light microscopy, cannot be excluded.

Finally, there is the possibility that the focal fibrosis of alveolar walls represents healed "rheumatic pneumonitis." Extravasation of fibrin into alveoli, frequently with the formation of "hyaline membranes" lining air spaces, is common in fatal cases of acute rheumatic fever,7 and probably is present to some extent in many nonfatal cases. The organization of this exudate, especially that applied to the walls of air spaces in the form of a hyaline membrane, could explain the focal increase in fibrous tissue in alveolar walls that sometimes accompanies mitral stenosis.

SUMMARY

Pathologic changes in alveolar walls have been described in the lungs of patients with mitral stenosis by many investigators. The purpose of this study is to establish the extent and character of such abnormalities of alveolar walls in 95 autopsied patients who died with mitral stenosis.

A study of microsections of the lungs of these patients reveals that pathologic alterations of alveolar walls are not frequent. Except for capillary dilatation, the changes are focal and affect only a small proportion of the area of lung examined. In 83 per cent of 95 patients even capillary dilatation was slight or absent.

These results suggest that advanced pathologic alterations of alveolar walls associated with mitral stenosis are in general only focal and are not extensive enough to be of physiologic significance.

SUMMARIO IN INTERLINGUA

Alterationes pathologic del parietes alveolar in le pulmones de patientes con stenosis mitral ha essite desribisce per multe investigatores. Le objectivo del presente studio es estableir le grado e le character de tal anormalitates del parietes alveolar in 95 necropsia patientes, morte con stenosis mitral.

Le studio de microsectiones del pulmones de iste patientes revela que alterationes pathologic del parietes alveolar non es frequente. A parte le dilatation capillari, le alterationes es focal e affice solmente un parve portion del area pulmonar examine. In 83 pro cento del 95 patientes, mesmo le dilatation capillari esseva leve o completamente absente.

Iste resultatos suggere que avantiate alterationes pathologic del parietes alveolar in association con stenosis mitral es generalmente solmente focal e non satis extense pro assumir signification physiologic.

REFERENCES

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