CHANGES IN THE LUNG AFTER LIGATION OF THE PULMONARY ARTERY AND INTRODUCTION OF A FOREIGN BODY INTO THE TRACHEA

N. V. Voikova

From the Department of Pathological Anatomy (Head – Prof. M. A. Zakhar'evskaya) of the I. P. Pavlov First Leningrad Medical Institute

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The changes in the lungs after ligation of the pulmonary artery began to be studied at the beginning of the twentieth century. Experimental investigations showed [21, 22, 11, 12, 19, 4, 13] the development of pneumosclerosis, the genesis of which remained uncertain. In addition the formation of bronchiectasis was observed, and in individual cases authors spoke out against the use of this operation in bronchiectasis [12, 13]. Some surgeons recognize the practical importance of the operation as an independent event, improving the general condition of the patient and leading to a reduction in the inflammatory manifestations in the lung [9, 1, 3, 14, 15, 16, 17, 18].

In view of the contradictory experimental and clinical findings and also of the inadequate number of systematic morphological investigations, we considered it timely to carry out an experimental investigation to study the changes in the lung tissue after ligation of the pulmonary artery; under these circumstances we directed our attention not only to the results of ligation in the course of their development but also to the special features of the course of the nonspecific inflammation arising in such cases.

EXPERIMENTAL METHOD

We carried out 2 series of experiments on rabbits weighing from 1.5 to 2.5 kg. In the first series of 26 rabbits the pulmonary artery was ligated, and in the second series of 16 rabbits, after ligation of the pulmonary artery a foreign body was introduced into the trachea. The pulmonary artery was ligated transpleurally; in conformity with existing indications [18] the artery was not divided. The rabbits were killed by air embolism at periods from 12 hours to 12 months. After the chest was opened, the trachea was ligated. The lungs were fixed in the opened pleural cavity in 10% formalin solution; after fixation, total preparations were made from each lobe of both lungs. The material was embedded in paraffin wax, and short series of sections (8-10) prepared from the lungs; from 15 to 200 sections were made from the trachea in the second series of experiments.

The following stains were used: hematoxylin-eosin, picrofuchsin by Van Gieson's method, the same method in conjunction with fuchsilin (for elastic tissue), mucicarmine, sometimes by Heidenhain's iron-hematoxylin, by the Gram-Weigert method, and in some cases by Foot's silver impregnation method.

EXPERIMENTAL RESULTS

In the first series of experiments no morphological changes were found in the right lung on macroscopic and microscopic examination. Both lobes of the left lung in the early stages were dark red in color, and later friable adhesions were present between them and the parietal pleura. Starting on the 10th day, the lung was reduced in size; its tissue was airless or rose-colored, and flabby. In the experiment, which lasted 12 months, the formation of bronchiectases was observed.

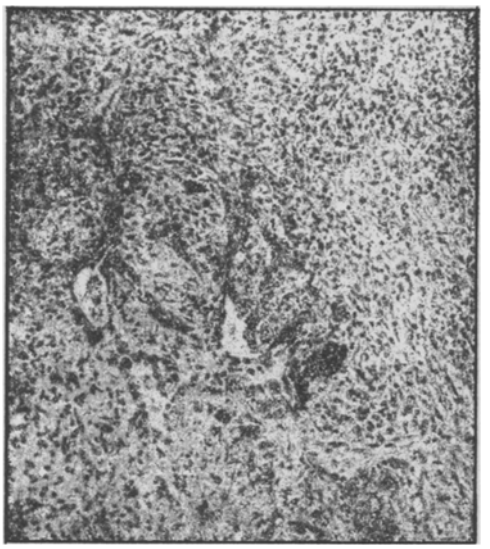

Fig. 1. Bands of indifferent epithelium from small caliber bronchi, in the form "whiskers." Stained with hematoxylin-eosin. First series of experiments. Time of experiment 7 days. Magnification: objective 16 ×, ocular 9 ×. (Zeiss).

Fig. 2. Proliferation of connective tissue in the walls of alveoli. The alveolar epithelium is in the form of layers of flattened and cubical cells. Van Gieson's stain. First series of experiments. Time of experiment 8 days. Magnification: ocular 6 ×, objective 16 × (Zeiss).

On microscopic examination it was found that after 12-24 hours the tissue of the left lung was aerated and in a condition of evenly distributed hyperemia; in places small hemorrhages were observed. On the 2nd and 3rd day, in addition, some pallor in the staining of the alveolar tissue could be noted. Later, on the 6th, 7th, 8th, 13th, 14th, 35th, 46th, 75th and 103rd days, an anemic infarct was found and this subsequently underwent organization.

The necrotic foci differed in size. Usually the center of the lobe became necrotic, occasionally the whole lobe; under these circumstances the wall of the main bronchus was often included in the necrosis. In the region of the focus of necrosis the cell muclei did not stain. The collagen fibers stained a pale color and their structure was indistict. The muscular coat of the vessels and bronchi appeared as a homogeneous mass, devoid of nuclei; the elastic and argyrophilic framework of the lung was preserved. Beneath the pleura a variable amount of lung tissue was preserved. The vessels in this zone had walls of the usual structure, and were filled with blood. Bands of connective tissue with large numbers of stretched-out blood vessels grew out toward the outer surface of the pleura. Around the foxus of necrosis, leucocytes formed a powerful barrier. Starting on the 8th day, outside the leucocyte barrier proliferation of connective tissue was observed, especially pronounced around the main bronchus. In and among the connective

Fig. 3. Organization of the lung parenchyma in association with diffuse proliferation of connective tissue. Tubes of stratified squamous and high cylindrical epithelium with mucous and a few leucocytes in the lumen. Infiltration of the connective tissue between the tubes with cells. Stained with hematoxylin and mucicarmine. First series of experiments. Time of experiment 131 days. Magnification: ocular 4 ×, objective 8 ×. (Zeiss).

tissue were seen remnants of the elastic framework of the lung, and also complex formations and bands of indifferent epithelium, round or elongated in shape (Fig. 1). In some of the complex formations a lumen could be distinguished; their epithelium became cylindrical or prismatic. Side by side with these complex formations were usually seen tubes of a regular, round or oval shape, lined with the same epithelium. If the wall of the lobar bronchus was included in the necrosis, its epithelium spread under the necrotic tissue, separating it from the tissue which was preserved, and at the same time formed processes which infiltrated the surrounding young connective tissue in the form of branching tubules. Around the periphery of the necrotic focus could often be seen thickened areas of connective tissue in the walls of the alveoli, with a well-marked epithelial lining at early stages this lining consisted of flattened epithelium, often even in the form of separate cells, and later of cubical epithelium.

In 8 cases no necrotic changes could be found in the lung tissue, and only diffuse and focal proliferation of connective tissue could be distinguished. On the 69th, 118th and 131st days, diffuse proliferation of connective tissue was found, so that the lobes of the lung were converted into adenoma-like tissue. The tubes were lined with cylindrical and prismatic epithelium, producing mucus; the lumen of the tubes contained a small number of leucocytes (Fig. 2). Between the tubes was a small amount of connective tissue, infiltrated by lymphocytes and histiocytes. Among the proliferating connective tissue were found vessels, filled with blood, with walls consisting of an elastic membrane and connective tissue. No arteriovenous anastomoses nor occluded arteries could be observed.

Foci of proliferation of connective tissue were seen on the 21st, 91st, 174th, 183rd, and 211th days, in the form of wedge-shaped or narrow scars containing adenoma-like formations and vessels similar to those described above in the case of the diffuse proliferation of connective tissue. The lung tissue surrounding the cicatricial foci was unchanged and in places emphysematous and filled with air. Arteriovenous anastomoses and occluded arteries were often found. With both focal and diffuse proliferation of connective tissue, numerous vessels could be seen in the commissures.

In the experiment, which was continued for 12 months, the tissue infiltrating the lobes was converted into large cavities containing leucocytes and lined with stratified squamous epithelium.

Histological examination of the pulmonary artery in the region of the ligature (12 cases) showed obliteration of its lumen by connective tissue and elastic fibers. From this description it was thus clear that after ligation of the pulmonary artery an anemic infarct was produced, with subsequent organization of the necrotic mass. The size of the scar evidently depended on the area of the preceding necrosis. After extensive areas of necrosis, the proliferation of connective tissue was diffuse and led to complete organization of the lung; small areas of proliferation terminated in focal pneumosclerosis.

If we accept the well-known scheme of the circulation in the lung [20], with slight modifications [10], then some idea may be gained of the circulation in the lung during the development of focal pneumosclerosis after ligation of the pulmonary artery. Blood from the bronchial artery passed through a system of arterial shunts into branches of the pulmonary artery, and partly through arteriovenous anastomoses into the venous system.

In addition blood reached the lungs through the commissures and pleural vessels. The arterial shunts presumably fulfil the role of arterio-arterial anastomoses. In diffuse pneumosclerosis the system of arterial shunts and arteriovenous anastomoses evidently did not come into action; the surviving lung tissue obtained its blood supply through its own particular bronchial artery and through vessels in the commissures and the pleura.

The second series of experiments consisted of a combination of ligation of the pulmonary artery and the introduction of a foreign body into the trachea. The foreign body, in the form of a sterile silk thread, was introduced into the trachea on the 14th, 92nd and 212th day after the operation of ligation of the pulmonary artery. As controls we used our experiments in which a foreign body was introduced into the trachea, described in a separate communication. At the level of the foreign body inflammation developed in the wall of the trachea; leucocytes and Gram-positive cocci accumulated in the lumen around the thread. In three cases, focal pneumonia was found in the right lung, and in the remainder bronchitis and hyperplasia of the lymphoid structures of the bronchi.

In the left lung, with the ligated pulmonary artery, inflammation developed against the background of the changes described above. In those cases when the anemic infarct was not yet successfully organized (introduction of the foreign body on the 14th and 92nd day after ligation of the pulmonary artery), bronchiectasis developed in the lung tissue (3 cases, Fig. 3), abscesses (1 case) and sequestration of the necrotic mass with a wide leucocyte barrier at the margin of the necrotic area (4 cases). In the experiments in which the necrosis had undergone organization (3 cases in which the foreign body was introduced on the 92nd day and 5 cases on the 212th day after ligation of the pulmonary artery), the changes were either indistinguishable from those described in the first series, or they consisted of some increase in the number of leucocytes in the lumen of the adenoma-like formations.

The results of both series of our experiments thus showed the possibility of infection via the bronchus of lung tissue, changed after ligation of the pulmonary artery. Infection was possible after ligation of the pulmonary artery alone, and even more so when this was combined with a foreign body in the trachea. In the latter case the conditions were more favorable for infection and the process of organization was complicated by suppuration, and sequestration and bronchiectasis usually arose.

The entire reorganization of the lung parenchyma which we observed in both series of experiments was of considerable interest. In the literature are descriptions of proliferation of tubes of cubical epithelium, referred to as pseudobronchi [13]. We have not found any more detailed description of these changes in the epithelium. In our experiments we also found proliferation of bands of indifferent epithelium as well as tubes of cylindrical, prismatic and stratified squamous epithelium. Evidently this was primarily proliferation of the epithelium of the bronchi, but there were grounds for the view that the epithelium of the alveoli also became modified. Nevertheless proliferation of the bronchial epithelium, if an inflammatory and regenerative character, was predominant. In the region of the necrosis in the wall of the main bronchus, the epithelium grew in a layer which crept over the living tissue and separated it from the necrosis. This type of growth was regenerative, but at the same time it could also be regarded as inflammatory growth, thanks to which delineation of the necrotic mass from the living tissue took place [6, 7, 8].

We were able to observe complete overgrowth of an extensive focus of necrosis connected to the wall of the main bronchus or a lobar bronchus. It is possible that bronchiectasis also developed as a result of this overgrowth. Around the intrapulmonary bronchi of varying calibar were found areas of epithelial proliferation, in the form of layers of indifferent epithelium and tubes of cylindrical and prismatic bronchial epithelium. Complete regeneration of the bronchi did not, therefore, take place; only a system of tubes was formed, connected to the residual bronchi.

We observed a peculiar reaction of the epithelium of the alveoli. At early stages, during proliferation of loose connective tissue in the wall of the alveolus, the alveolar epithelium could be seen in the form of a layer of flattened epithelial cells; at later stages, during conversion of the connective tissue into scar tissue, the alveolar epithelium became cubical. This accomodation of the alveolar epithelium was associated with the interference with its function and also with the change in the state of the underlying tissue, i.e. it was the result of disturbance of the unity of the physiological system "epithelium - connective tissue" [7, 8, 5].

SUMMARY

Experiments with the ligature of the pulmonary artery were conducted in 26 rabbits. An anemic infarction with subsequent organization and development of focal and diffuse pneumosclerosis was obtained. Inflamatory and regenerative proliferation of the bronchial epithelium in the form of indifferent bands and the layer demarcating the necrosed tissue was observed together with the proliferation of the connective tissue.

Besides there is seen an appearance of the alveolar epithelium with its transformation into cubic epithelium. Combination of the pulmonary artery ligature with introduction of a foreign body into the trachea (16 rabbits) resulted in more intense inflammation. The development of bronchiectasis was noted in 2 cases and sequestration of necrosed masses – in 3.

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