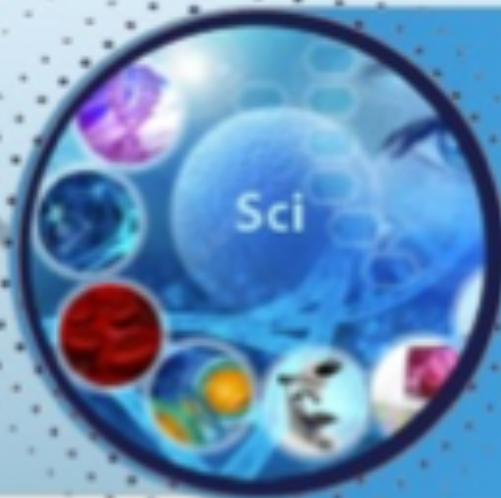




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Clinical and Morphological Characteristics of Acute Purulent-Destructive Lung Diseases

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ABSTRACT

Patients with acute abscesses and lung gangrene have certain associated changes in the large bronchi of the catarrhal and sclerotic bronchitis, with a predominance of dystrophic changes, exposure of basal cells, enlargement of intercellular spaces and instability of the bronchial epithelium, which is manifested by the proliferation of goblet cells and a nested change in the functional activity of the cells of the epithelial layer. The possibility of forming three morphological variants of the restructuring of the respiratory spine in patients with purulent-destructive lung diseases, depending on the peculiarities of the course of the processes of fibrinogenesis and fibrinostabilization, the activity of phagocytic cells and the nature of the restructuring of the microcirculatory bed. Structural-spatial reorganisation of the basement membranes of the alveolar epithelium and the endothelium of blood vessels in patients with acute abscesses and gangrene of the lungs proceeds in the form of splitting and destruction. The nature of restructuring the microcirculatory bed of the respiratory section in patients with acute abscesses and gangrene of the lungs is stereotypical, and the degree of severity of morphological changes depends on the clinical variant of the course of purulent-destructive lung diseases.

Keywords: lung abscess, lung gangrene, chronic bronchitis

INTRODUCTION

The persistence of a high incidence of acute purulent-destructive lung diseases, low quality of life in them, high mortality and disability determine the urgency of the problem of their treatment [1, 5].

Clinical and morphological studies conducted in recent years have shown that the nature of the course of acute purulent-destructive lung diseases is largely determined by the reactivity of the macroorganism [2, 8].

In the pathogenesis of purulent-destructive lung diseases, there are three main links, the interaction of which determines the course of the disease: impaired bronchial

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permeability, an acute infectious inflammatory process in the pulmonary parenchyma, and impaired blood flow in the microcirculatory system, leading to the destruction of lung tissue [3, 6].

Blockade of microcirculation in the affected area and intensive deposition of fibrin both in the microvessels of the organ and in the surrounding interstitial tissue of the lung leads not only to the development of ischemic and inflammatory disorders but also impedes the access of drugs to the focus of destruction, which reduces the effectiveness of treatment and causes destabilisation of cell-stromal interactions in the lesion [4,7, 9].

On the other hand, the failure of the primary fibrin block leads to the progression of the inflammatory process and the involvement of new anatomical structures of the lungs, which negatively affects subsequent reparative processes due to the presence of a predominantly intracellular form of regeneration in the respiratory part of the lungs.

At the same time, the issues of structural reorganisation of the respiratory part of the lungs in connection with the processes of fibrin formation and fibrinostabilization, changes in the functional activity of cell populations of the inflammatory infiltrate, and restructuring of the microcirculatory bed remain insufficiently studied. This substantiates the expediency of the above directions in the study of the problem of acute purulent-destructive lung diseases. In this regard, the purpose of our study was to increase the diagnostic significance of pathomorphological studies of purulent-destructive lung diseases.

MATERIAL AND METHODS

The work was based on data from 175 patients, including 129 patients with acute lung abscesses, 22 patients with pulmonary gangrene, and 24 patients with chronic bronchitis. Among patients with purulent-destructive lung diseases, there were 128 (84.8%) men and 23 (15.2%) women. The age of patients ranged from 22 to 80 years, with an average of 51.8 ± 11.8 years (standard mean error 1.1). Among patients with chronic bronchitis, there were 20 (83.3%) men and 4 (16.7%) women aged 22 to 77 years; the mean age was 47.6 ± 2.31 years.

The criteria for excluding patients with pulmonary destructive processes from the study were lung destruction of specific aetiology (tuberculosis, syphilis) and lung cancer accompanied by destruction of the pulmonary parenchyma. By the objectives set in the study, a morphological study of bronchial biopsies of large

bronchi was carried out in 35 patients aged 32 to 65 years with acute abscesses without sequestration (28 patients), acute abscesses with sequestration (4 patients) and gangrene (3 patients) of the lungs. They made up the main group. The comparison group included 24 people suffering from chronic bronchitis. To assess the nature and severity of morphological changes in the respiratory part of the lungs in purulent-destructive lung diseases, 116 studies (95 men and 21 women aged 24 to 80 years) of the tissues of the respiratory part of the lungs were carried out. Depending on the clinical form of the course of purulent-destructive lung diseases, observations were divided into two groups. The first group consisted of 97 patients with acute abscesses, including 69 patients with acute lung abscesses without sequestration and 28 patients with acute abscesses without sequestration. The second group included 19 patients with pulmonary gangrene.

Histological treatment of tissues was carried out according to the generally accepted method, sections with a thickness of 4-6 μm were stained with hematoxylin and eosin, Weigert's picrofuchsin, according to Gordon-Sweet, according to the method of A.N. Yatskovsky, a CHIC reaction was performed. To assess the processes of fibrin formation and fibrinostabilization, the Picrot-Mallory fibrin stain and the MSB method were modified by D.D. Zerbino were used.

To determine the expression of type IV collagen and podoplanin, the method of double indirect immunofluorescence was used. The following antibodies were used as primary antibodies: monoclonal antibodies to collagen type IV (C-1926, "Sigma", dilution 1:100), rabbit polyclonal antibodies to podoplanin (P-5374, "Sigma", dilution 1:10). Texas-Red tagged goat antibodies (XR-9770, "ProSci" diluted 1:20) were used as secondary antibodies for visualisation of type IV collagen, and FITS-labeled antibodies (F-9887, Sigma, diluted 1:1000) were used for podoplanin visualisation.

For the study, a Zeiss Axioscop 40 microscope (Carl Zeiss, Germany) was used, equipped with an HBO-100W mercury lamp as a light source. For fluorescence, filter set 00 (BP 530-585), filter set 09 (BP 450-490), and Carl Zeiss (Germany) filters were used.

Morphometric studies were carried out using the ImageJ 1.34 and AxioVision 3.1 (Carl Zeiss, Germany) graphics packages.

The data obtained were processed statistically using computer programs JMP 5.1 SigmaStat 3.10 for Windows. The level of statistical significance was $p < 0.05$.

RESULTS AND DISCUSSION

In conditions of acute purulent destruction, morphological changes in large bronchi of the type of catarrhal or sclerosing bronchitis were noted, with an excess of the frequency of these changes in chronic bronchitis. The frequency of catarrhal-sclerosing forms of bronchitis in purulent-destructive lung diseases was less than in patients with chronic bronchitis.

In the integumentary epithelium of large bronchi of patients with purulent-destructive lung diseases, the ciliated border was often disturbed, and the number of goblet cells was normal or moderately increased. Signs of focal hyperplasia of goblet cells were noted in 28.6% of cases and basal cells in 17.1%. In patients with chronic bronchitis, there were few goblet cells; their hyperplasia was noted in 8.3% of cases, while pronounced focal hyperplasia of basal cells was observed in 50% of cases.

In the conditions of the development of acute purulent destruction in the integumentary epithelium of the large bronchi, dystrophic changes prevailed (68.6%). In 60% of cases, the disintegration of epithelial layer cells with the formation of interepithelial cavities was determined. A cluster decrease in the functional activity of epithelial cells was noted.

Functional activity was retained by $26.8 \pm 4.32\%$ of epithelial cells. The basement membrane was homogenised, of uneven thickness, averaging $4.82 \pm 0.16 \mu\text{m}$. Polymorphic subepithelial infiltration was characterised by low intensity and focal character.

Patients with chronic bronchitis were characterised by atrophic changes in the epithelium (45.8%). Nevertheless, the functional activity of epithelial cells was reduced to a much lesser extent than in patients with purulent-destructive lung diseases: $68.4 \pm 5.67\%$ of epithelial cells remained functionally active.

An increase in the intercellular spaces between the epithelial cells of the integumentary epithelium was noted much less often than in patients with purulent-destructive lung diseases (8.3%).

A thickened, sclerosed basement membrane of the epithelium was noted, its thickness averaged $8.13 \pm 0.3 \mu\text{m}$. Subepithelial polymorphocellular infiltration with a predominance of macrophages and lymphocytes was determined. Expansion of microcirculatory bed elements and lymphatic capillaries against the background of sclerotic changes in the lamina propria was revealed.

Thus, in the biopsies of large bronchi of patients with acute abscesses and lung gangrene, morphological changes of the type of catarrhal or sclerosing bronchitis predominated. At the same time, dystrophic changes,

exposure of basal cells, the disintegration of epithelial cells and enlargement of intercellular spaces, and instability of the bronchial epithelium, which was manifested by a proliferation of goblet cells and nested changes in the functional activity of cells, prevailed in the integumentary epithelium. The basement membrane was moderately thickened, of uneven thickness, and homogenised.

In patients with acute lung abscesses, the clinical picture was characterised by chest pain in 65% of patients who cough with sputum secretion in 94.9%. All patients noted anorexia, weakness, fatigue, and shortness of breath. In 92.8% of patients, body temperature was elevated. In 55.7% - the body temperature was from 37°C to 38°C , in 30.9% - 38°C and above. 67.0% had weight loss. Plasma protein below 65 g/L was observed in 29.9% of patients. All patients showed high activity of the inflammatory process according to laboratory methods, high ESR values (in 48.5% more than 40 mm/h, maximum value 75 mm/h), C-reactive protein, fibrinogen, leukocytosis, and a shift of the leukocyte formula to the left. In the majority (56.7%) of patients, the right lung was affected, and the left lung suffered less often - in 30 (30.9%) patients. The lower lobe of the right lung was affected more often (28.9%), and the upper lobes of the right and left lungs were affected by the pathological process approximately equally often (11.3% and 10.3%, respectively). Bilateral lung suppuration was diagnosed in 12 (12.4%) patients.

In 41.3% of patients, the condition was severe (33%) and extremely severe (8.3%) upon admission. 11.3% had a mild degree of severity, and 47.4% - moderate severity.

In the analysed group, 43 patients had complications. 39.2% of patients had pyopneumothorax and pleural empyema, 12.4% had sepsis, 7.2% had a pulmonary haemorrhage, and 3.1% had phlegmon in the chest wall.

Morphological examination made it possible to identify three variants of pathohistological reorganisation of the respiratory region in patients with acute lung abscesses. These structural variants had distinctive features depending on the degree of severity of fibrin formation and fibrinostabilization, the functional state of the cell populations of the inflammatory infiltrate, and the nature of disorders of the microcirculatory bed of the respiratory part of the lungs.

The first morphological variant was observed in 58% of patients with acute lung abscesses without sequestration and in 7.1% of patients with acute lung abscesses with sequestration. The focus of purulent destruction was well limited from the surrounding tissues by "young"

fibrin deposits, with a fibrin formation period of 2 to 48 hours. Inflammatory cell infiltrate contained $61.8 \pm 2.19\%$ neutrophils, $33.4 \pm 0.97\%$ macrophages, and $4.760.1b\%$ lymphocytes. In the area of the fibrin block, the formation of microcavities around the cell populations of the inflammatory infiltrate was observed.

The membrane receptors of macrophages, neutrophils, and lymphocytes were not blocked by fibrin deposits, and thus, the cells were able to perform their inherent biological functions.

$61.7 \pm 2.21\%$ of macrophages, $82.1 \pm 3.08\%$ of neutrophils, and $89.5 \pm 2.39\%$ of lymphocytes retained functional activity.

The microvessels in the area of limitation of the acute purulent-destructive focus were full-blooded. In their lumen, the presence of fibrin deposits was not noted, only in isolated cases a delicate network of "young" fibrin was observed in the hemocapillaries on the surface of leukocytes.

Thus, the patency of blood vessels for the formed elements of blood was preserved. The relative cross-sectional area of the vessels was $14.7 \pm 1.09 \mu\text{m}$, and the number of vessels per unit area was 3.45 ± 0.37 .

Immunohistochemical verification of type IV collagen revealed local sites of cleavage and destruction of the basement membranes of alveolocytes and endotheliocytes. Fixation of basement membrane fragments on the fibrin matrix was noted.

The vessels of the deep lymphatic system of the lung were well visualised. Lymphatic vessels that were in the focus of purulent destruction or on the border with it were subjected to the greatest damage. Exfoliation of the endothelium of lymphatic vessels, deformation and destruction of their walls were determined. Lymphatic vessels located in the zone of restriction and in more distant areas, as a rule, retained their morphological structure.

All patients with the presented variant of morphological transformations of the respiratory region noted chest pain, pronounced signs of respiratory failure were observed (an increase in respiratory rate of more than 22 per minute in 84.1% , cough with sputum secretion in 95.7% , including in 30.4% - more than 200 ml per day) and moderately pronounced signs of intoxication syndrome (body temperature of more than 38°C was observed in 31.9% , Systolic blood pressure less than 100 mm Hg. st. - in 33.3% of patients).

The second morphological variant was observed in the overwhelming majority of cases (85.7%) of patients with acute lung abscesses with sequestration and in

26.1% of patients with acute lung abscesses without sequestration.

In the respiratory part of the lung, the prevalence of fibrin formation processes over fibrinolysis was noted. At the same time, there was a pronounced limitation of the purulent-destructive focus by "young" and "maturing" fibrin. In the area of the fibrin block, fibrin deposits formed a dense network into which the cell populations of the inflammatory infiltrate were literally "mounted". It contained a moderate number of neutrophils and macrophages ($54.8 \pm 1.64\%$ and $44.2 \pm 1.46\%$, respectively) and an insignificant content of lymphocyte cells ($0.98 \pm 0.03\%$). Such closure of cells in a "fibrin cocoon", blocking their functional activity, led to the impossible elimination of "young" and "young" fibrin, its maturation and the development of sclerotic changes. Functional activity was retained in $58.8 \pm 2.22\%$ of neutrophils, $49.8 \pm 1.38\%$ of macrophages, and $60.8 \pm 1.73\%$ of lymphocytes.

In the lumen of blood vessels, massive fibrin deposits were determined, with impaired patency of blood vessels. Exfoliation of the endothelium, swelling of the vessel wall, its infiltration by lymphohistiocytic cells, and conglomerates of mononuclear cells in the lumen of the vessels were noted.

The relative cross-sectional area of the vessels was $9.68 \pm 1.23 \mu\text{m}$, the number of vessels per unit area was $3.63 \pm 0.69 \mu\text{m}$. Splitting and destruction of basement membranes were extended, occupying from 20 to 50% of the circumference of microvessels. In some cases, pronounced destructive changes in basement membranes were observed with the preservation of collagen-IV positive structures in the form of globules.

Lymphatic vessels were visualised in a smaller number, and extended changes in the vascular wall in the form of deformation and exfoliation of endothelial cells were noted.

The clinical picture of the course of the disease in the above-described morphological variant was characterised by blurred symptoms of the manifestation of the disease. Chest pain was noted in 57.1% of patients, in 60.7% , the amount of expectorated sputum per day was less than 200 ml, and tachypnea was more than 22 per minute - in 32.1% . Signs of intoxication syndrome (tachycardia - 92.9% , decrease in systolic blood pressure - 67.8% , increase in body temperature over 38°C - 53.6%) were pronounced.

The third morphological variant was observed in 15.9% of patients with acute lung abscesses without se-

questration and in 7.1% of patients with acute lung abscesses with sequestration. At the light-optical level, there was a weakly pronounced limitation of the focus of destruction with the weak formation of a fibrin block from "young" fibrin deposits. Populations of the inflammatory infiltrate did not close in a fibrin cocoon. The functional activity of macrophages was significantly reduced ($49.1 \pm 2.83\%$) against the background of relatively preserved or increased activity of neutrophils and lymphocytes ($63.9 \pm 3.53\%$ and $82.5 \pm 3.81\%$, respectively).

The vessels of the microcirculatory bed remained patency in most cases. The walls of blood vessels and perivascular tissues of the lung underwent sclerotic changes.

Patients with this variant of morphological transformations of the respiratory part of the lungs were characterised by a severe course of the disease; often, the process took on a widespread or bilateral character. There was a pronounced pain syndrome (in all patients), pronounced signs of respiratory failure (tachypnea in 76.9% of patients, cough with significant sputum discharge of more than 200 ml per day in 69.2%) and intoxication (tachycardia in 92.3%, a decrease in systolic blood pressure less than 100 mm Hg in 84.6%, an increase in body temperature and high activity according to laboratory research methods in all patients).

Most patients with pulmonary gangrene noted an acute onset of the disease, with an increase in body temperature to febrile figures, the appearance of a cough with fetid sputum, and chest pain aggravated by breathing and coughing. Patients associated the onset of the disease with hypothermia, previous colds and contact with patients with acute respiratory viral infections.

All patients with pulmonary gangrene noted chest pain, which was accompanied by cough with fetid sputum, weakness, fatigue, shortness of breath, and decreased appetite. At the same time, in 4 (21.1%) patients, it ranged from 37°C to 38°C , in 12 (63.2%), it ranged from 38° to 39°C , in 3 (15.8%), it exceeded 39°C . The heart rate in 10 (52.6%) patients exceeded 110 beats per minute. The level of systolic blood pressure in 13 (68.4%) was below 100 mm Hg. Respiratory rate more than 22 times per minute was recorded in 16 (84.2%) patients. In all patients with pulmonary gangrene, a high activity of the inflammatory process was noted according to laboratory research methods (high ESR values - in 11 (57.9%) from 44 to 70 mm/h, C-reactive protein, fibrinogen, leukocytosis, shift of the leukocyte formula to the left).

In 9 (47.4%) patients, gangrene was localised in the right lung, and in 8 (42.1%) - in the left. Bilateral localisation of the pathological process was noted in 10.5% (2 patients) of cases. In the right lung, the pathological focus was more often localised in the lower lobe (21.1%), in the left lung, there was a more frequent lesion of both lobes - 15.8%.

In 5 (26.3%) patients, there were complications from the pleural cavity. Pulmonary haemorrhage was recorded in 5 (26.3%) patients.

Contralateral pneumonia was observed in 4 (21.1%) patients; 5 (26.3%) patients were extremely severe, 10 (52.6%) were severe, and four patients (21.1%) were diagnosed with moderate severity.

Morphological examination of cases of lung gangrene in the respiratory region of the lung showed a tendency to an accelerated transition of "young" and "young" destructions, which were vaguely limited from the surrounding lung tissues by a small amount of "young" fibrin into more mature forms. Purulent exudate contained a large number of necrotically and necrobiologically altered neutrophils ($64.4 \pm 1.52\%$) with a moderate ($34.4 \pm 1.16\%$) and negligible ($1.16 \pm 0.04\%$) number of macrophages and lymphocytes.

The grid arrangement of fibrin deposits was determined. Phagocytic cells (a large number of neutrophils and a moderate number of macrophages) did not close in a fibrin cocoon. However, the functional activity of macrophages was significantly reduced ($48.7 \pm 1.20\%$) against the background of preserved or increased activity of neutrophils and lymphocytes ($65.0 \pm 1.97\%$ and $74.0 \pm 2.05\%$, respectively).

In the lumen of blood vessels, multiple fibrin-erythrocyte thrombi were observed, in some cases with the phenomena of organisation and revascularisation. Exfoliation of the endothelium divergence of elastic elements of blood vessels was noted. Significant structural changes in the basement membranes of the alveolar epithelium and blood vessels in the form of splitting and destruction were observed.

The relative cross-sectional area of the microcirculatory bed in the total number of observations was the smallest and amounted to $8.93 \pm 0.73 \mu\text{m}$, the number of vessels per unit area was $3.37 \pm 0.79 \mu\text{m}$. The blood supply to the region of destructive changes was statistically significantly reduced in comparison with the indicators of patients with acute lung abscesses.

Significant morphological changes in the vessels of the deep lymphatic system of the lung, exfoliation of the

endothelium, deformation of the lumen of the vessel, and destruction of the vascular wall were noted.

CONCLUSION

In acute abscesses and gangrene of the lungs, the associated changes in the large bronchi are mainly catarrhal and sclerosing forms of bronchitis, which contribute to the disruption of the drainage function of the bronchi and precede the development of purulent-destructive lung diseases. In the integumentary epithelium of the bronchi, dystrophic changes, exposure of basal cells, disintegration of epithelial cells and enlargement of intercellular spaces, proliferation of goblet cells and clustered changes in the functional activity of epithelial cells predominate. In patients with acute lung abscesses in the respiratory region, three variants of structural and functional disorders are revealed due to the peculiarities of the processes. Fibrin formation and fibrinostabilization, the activity of cell populations of inflammatory infiltrate and patency of microcirculatory vessels, complete limitation of the focus of acute purulent destruction by young fibrin, preservation of patency of blood vessels and activity of phagocytic cells, free arrangement of phagocytes.

In patients with lung gangrene, the fibrin block is not clearly expressed, there is a tendency for an accelerated transition of young fibrin deposits into more mature forms, and the functional activity of macrophages is reduced against the background of maintaining the activity of neutrophils and lymphocytes, the blood supply to the region of destructive changes is statistically significantly reduced, compared to patients with acute lung abscesses. Changes in the basement membranes of the alveolar epithelium and the endothelium of blood vessels in the form of splitting and destruction are most pronounced.

Conflict of Interest – None

Ethical aspect – the article is reviewed, and the information presented has a cited reference to primary sources.

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