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Morphological Changes In Mucous Membrane Of Bronchi In Patients With Severe Chronic Obstructive Pulmonary Disease

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Chronic obstructive pulmonary disease (COPD) and in the twenty-first century remains a major global health problem, resulting high rates of morbidity and mortality. In the past two decades important progress has been made in the understanding of the epidemiology, pathophysiology, diagnosis, and treatment of COPD, but still there is a lack of fundamental knowledge about the cellular, molecular and genetic causes of disease.
Remodeling of respiratory tracts is a pathologic process observed at chronic inflammatory and obstructive diseases of respiratory tracts. For the study 9 people with severe COPD with the periods of 1, 3 and 6 months were performed biopsies of the mucous membrane of the bronchi. Verification of the diagnosis and its formulation confirmed with the orders of Ministry of Health of Ukraine № 128 from 19.03.2007. "On approval of clinical protocols of medical care in the specialty pulmonology".

Keyword: Chronic Obstructive Pulmonary Disease, Airway Remodelling, Factors Protect Mucosal.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is now recognised to be a condition of global importance because of high morbidity and risk of premature death of millions of people. At present, COPD is considered as a multicomponent disease with multiple extrapulmonary effects that in some cases determine the prognosis for patients [3]. In the past two decades important progress has been made in the understanding of the epidemiology, pathophysiology, diagnosis, and treatment of COPD.

COPD is primarily characterized by the presence of airflow limitation as a result of inflammation and airway remodeling and is often associated with the destruction of the lung parenchyma and the development of emphysema. Symptoms of COPD include chronic cough, excessive sputum production, wheeze, shortness of breath and chest tightness. COPD is caused by long-term inhalation of harmful gases and particles, such as cigarette smoke, the risk of COPD increases during exacerbations [9].

It is increasingly recognized that COPD beyond the lungs , and that many patients have several systemic manifestations, which may further impair the functionality and quality of life [10]. In addition, increasingly COPD associated with several other diseases such as cardiovascular disease, osteoporosis, diabetes, and metabolic syndrome. Systemic effects and comorbidities in patients with COPD increases the risk of hospitalization and mortality and the cost of their treatment [10].

The burden of disease is particularly high in developing countries [9]. According to official statistics, in Ukraine, the incidence of COPD is 10 times higher than in bronchial asthma. In percentage terms, COPD (62.4%) is far ahead of other respiratory diseases for the duration of periods of disability in the structure of bronchopulmonary disease (compared to asthma - 21.4%, pneumonia - 7.6%) [1, 2, 5, 8].

WHO experts estimate that today moderate-to-severe COPD have 80 million people [4]. More than 3 million people died of COPD in 2005, which is equal to 5% of all deaths globally [1-5]. Every hour COPD kills more than 250 people - that is, every 15 seconds somewhere in the world someone dies from COPD [1-4]. The financial costs associated with COPD, only in the European Union account for more than 10 billion euros per year. An estimated 3 million people have chronic obstructive pulmonary disease (COPD) in the UK. COPD is a major health issue in the UK and is the fifth leading cause of death, currently accounting for 26,000 to 30,000 deaths per year. It is the second most common reason for emergency hospital admissions in the UK, with 1 in 8 emergency admissions each year being due to COPD [12-14].

This pathology was the cause of 2.7% of all deaths, although, according to experts, mortality from COPD is clearly underestimated. In Russia in 2004 of 37,806 people died of COPD [7]. WHO experts say that over the past 30 years, mortality from COPD in the world has increased by 163%. [6] Thus, this disease is found in 4-6% of the adult population of Europe. Moreover, the number of patients in the UK is around 3,000,000 people., Germany - 2.7 million in Italy and France - 2.6 million in Spain - 1.8 million [2].

In European countries about 74% of all costs associated with COPD are wasting on disability patients and less than 20% are the direct costs of their treatment (about 12% for outpatient, and 7% - Landline) [1-2]. However, today the cost of COPD in general is three times higher than the cost of bronchial asthma (BA).

It is currently accepted that an inflammatory response of the lungs is a key pathogenic mechanism in COPD, this inflammatory response is characterised by: 1) increased numbers of neutrophils, macrophages and T-lymphocytes with a CD8+predominance; 2) augmented concentrations of proinflammatory cytokines, such as leukotriene B4,interleukin (IL)-8 and tumour necrosis factor (TNF)-a, among others; and 3) evidence of oxidative stress caused by the inhalation of oxidants (tobacco smoke) and/or the activated inflammatory cells mentioned above [11].

Remodeling of respiratory tracts is a pathologic process observed at chronic inflammatory and obstructive diseases of respiratory tract. According to P.K. Jeffery (2004) fibrotic changes play important role in airways remodeling [16-18]. Knowledge about airway remodeling in COPD is still limited and we believe that the effectiveness of any disease treatment depends on a deep knowledge of all parts of its pathogenesis.

2. Material and Methods

For the study 9 people with COPD III stage with the periods of 1, 3 and 6 months were performed biopsies of the mucous membrane of the bronchi. Verification of the diagnosis and its formulation confirmed with the orders of Ministry of Health of Ukraine № 128 from 19.03.2007g. "On approval of clinical protocols of medical care in the specialty pulmonology" [4].

The material of the research was bronchoalveolar lavage and bronchial biopsy materials received on the level of bifurcation of proximal bronchi to segmental bronchi during fiberoptic bronchoscopy.

3. Results

In the pseudostratified epithelium of the mucous membrane of a bronchus it was observed a thickening of the basement membrane. The thickness of epithelium on the perimeter was not the same. The areas with low epithelium alternated with pavement epithelium and a complete absence of epithelial cells and denudation of the basement membrane. In the epithelial layer it was difficult to separate basal and intercalary cells. Goblet cells were barely distinguished. On the surface of epithelium in the preserved areas the cilium were not found and the clots of mucus were localized.

In lamina propria of mucous membrane of a bronchus it was observed a great number of mighty bundles of collagen fibers. Cell population was presented by a great number of myofibroblasts that were defined by an irregular shape with pointed processes, basophilic cytoplasm, and a big rounded nucleus with hyperchromic chromatin. Myofibroblasts are inclined to torsion in deep areas of lamina propria. Between them there are a lot of macrophages (often with granules in cytoplasm) and lymphocytes. There are few fibroblasts. Inflammatory polymorphocellular infiltration was not identical in the visual field. The lumen of blood vessels is dilated and often contained blood corpuscles, their wall is thinned. In the vessels of microcirculation bed there are stases. Often the cellular infiltration dominates in perivascular areas.

In one case there was discovered a proliferation of epithelium with formation of microfolds of superficial epithelium with subordinate lamina propria.

The electronic microscopic picture was characterized by the signs of chronic inflammatory process. In epithelial cells that were found in the section, a picture of necrosis was often observed. Plasmolemma of an epithelial cell did not contour and its content conjugated with amorphous substance of the subordinate connective tissue. In cytoplasm there are numerous transparent vacuoles, remains of organelles, amorphous structures.

On the transverse section it was observed dilatation and weakening of intercellular contacts with dilatation of intercellular spaces. In one viewing field it was observed a section of cells in their nuclear and anucleate parts. Separate nuclei contained nucleoli. Cytoplasm is homogeneous, organelles are hard to identify. Goblet cell is in the necrobiotic condition with kariopicnoti nucleus. In its enclosing epithelial cells are deeply damaged.

In fibroblasts of the subordinate connective tissue the nucleus is big, chromatin is moderately and evenly condensed throughout the whole nucleus. In cytoplasm there are identified mitochondria, endoplasmic reticulum, and beyond the cells – the products of fibrillogenesis – pro- and microfibrils, elements of amorphous substance. Such fibroblasts occur not often.

More widespread in the connective tissue are myofibroblasts. These cells are localized in the shape of groups of a few cells. The cells bodies are of lengthened fusiform form, the nuclei are lengthened with peripheral condensation of chromatin. In cytoplasm there are identified numerous microfilaments, and separate mitochondria. In the environment of the cells it is observed thick collagen fiber bundles oriented in different directions.

In the inflammatory infiltration there are quite a lot of macrophages. In the nucleus there is a peripheral condensation of chromatin. It contains two fragments of a nucleus. Plasmolemma does not have contours clarity. Numerous twisted processes are coming from the body and that is why there are a lot of their fragments near the cells. In cytoplasm there are big phagosomes one of which is a giant one. Their content is fragments of membrane organelles and thickened osmiophil material. In other areas the cytoplasm is homogeneous, single organelles are barely seen (cisterns of endoplasmic reticulum, mitochondria with shortened cristae). Around the macrophage there is the basic (amorphous) substance of the soft connective tissue in the state of edema.

What attracts attention is that among the cells of inflammatory infiltration in the connective tissue there are few plasmocytes. Plasmocytes show considerable destructive changes. In a nucleus it can be often observed an edema with eccentric displacement of chromatin. In cytoplasm degranulation of rough endoplasmic reticulum, single mitochondria. Primary lysosomes are identified seldom, more often secondary – phagosomes and tertiary - residual corpuscles. Plasmolemma is contoured not clearly.

In many blood capillaries in dilated lumen there is a stasis of blood corpuscles mostly erythrocytes. The basement membrane is thickened and damaged in some places. In the nucleus of endotheliocyte there is a peripheral condensation of chromatin. In the peripheral area of the endotheliocytes cytoplasm is difficult to

identify the organelles, but mitochondria and phagosomes are distinguished.

Around the capillaries there are considerable layers of collagen fibers. In the surrounding of the capillary there are observed myofibroblasts and their processes, bundles of collagen fibers that have different directions and maturity.

Sometimes the thickening of the basement membrane and surrounding of the capillary by collagen fibers is considerably expressive. The capillaries have fissural lumen and are "embedded" into the bundles of connective tissue that have circular localization. Endotheliocyte of the capillary wall has pyknotic nucleus and thinned electronically thickened cytoplasm. In lamina propria of mucous membrane there is an evident pulmonary fibrosis, there are myofibroblasts and mighty bundles of collagen fibers. Myofibroblasts in the wall in allergic bronchial irritation have been described by W.R. Roche *et al* [15].

In some capillaries the lumen is free from blood corpuscle but endotheliocytes are in the state of destruction (necrosis). Their cytoplasm is electronically thickened and has vacuoles. The basement membrane is identified only in separate areas. The capillary is surrounded by collagen fibers situated as tight laminae. From the outside of them there are collagen fibers on the transverse section, i.e. collagen fibrous structures have two layers – circular and longitudinal. Near the nucleus-containing area of endotheliocyte the collagen fibers have reticular form and are less dense and thick.

4. Conclusions

(i) In severe COPD damaged bronchial mucosa with a significant growth of connective tissue in the lamina propria of clearly identifiable basement membrane alteration, the presence of fibroblasts, activation of fibroblasts / myofibroblasts and mucous glands are determined

(ii) The identification of inflammatory mediators, and understanding the morphological changes are important for the development of anti-inflammatory treatments that may reduce the inflammation and reduce the clinical symptoms of COPD.

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