histopathological markers such as ulceration and mitotic rate, provides valuable prognostic and therapeutic insights. The findings suggest that personalized treatment strategies incorporating targeted therapy and immunotherapy can significantly improve patient outcomes. Future research should focus on refining molecular classification systems and exploring novel therapeutic combinations to overcome treatment resistance in high-risk melanoma subtypes.

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M. N. Fathima Farhana, U. C. Christian

Scientific supervisor: MD, PhD G. V. Tishchenko

Educational Establishment
«Gomel State Medical University»
Gomel, Republic of Belarus

HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL ANALYSIS OF EMPHYSEMA SUBTYPES: PATTERNS OF LUNG DAMAGE

Introduction

Emphysema is a chronic pulmonary disease marked by abnormal, permanent expansion of air spaces distal to the terminal bronchioles and alveolar wall destruction without significant fibrosis. This process reduces elastic recoil, leads to air trapping, and impairs gas exchange. It is a major component of chronic obstructive pulmonary disease (COPD). The progression of emphysema is driven by multiple etiological factors, the most prominent being smoking, which induces oxidative stress, inflammation, and a protease-antiprotease imbalance. Exposure to cigarette smoke activates neutrophils and macrophages, triggering the release of elastase and matrix metalloproteinases, leading to the degradation of elastin and extracellular matrix components. Additional environmental and occupational exposures, including prolonged contact with air pollution, biomass fuel, and industrial chemicals, contribute to disease progression. Individuals with prolonged exposure to coal dust, silica, and other particulates demonstrate accelerated lung damage. Genetic predisposition, particularly α1-antitrypsin deficiency, allows unchecked protease activity, predominantly affecting the lower lobes and leading to panacinar emphysema. Aging and recurrent infections further exacerbate emphysema, as reduced alveolar elasticity and capillary rarefaction make the lungs more vulnerable to structural damage.

The prevalence of emphysema varies geographically. According to the Global Burden of Disease Study 2019, the prevalence of COPD in Belarus is estimated at 4.5% among individuals over 30 years of age, whereas in industrialized nations such as India and China, emphysema prevalence ranges between 9–15% and 8–12%, respectively. Declining trends have been observed in the United States and the United Kingdom due to the implementation of anti-smoking campaigns and air quality regulations.

Morphologically, emphysema presents with distinct macroscopic and microscopic features. Gross examination reveals hyperinflated lungs that do not collapse when removed from the thoracic cavity, bullae larger than 1 cm that predispose individuals to spontaneous pneumothorax, and a flattened diaphragm contributing to a barrel chest appearance. Microscopic examination distinguishes various subtypes of emphysema. Centriacinar emphysema, primarily affecting the upper lobes, is associated with smoking and involves the destruction of respiratory bronchioles while sparing distal alveoli. Panacinar emphysema results in uniform acinar destruction, predominantly in the lower lobes, and is linked to α1-antitrypsin deficiency. Paraseptal emphysema, characterized by bullae formation, primarily affects distal alveoli and is observed in both smokers and idiopathic cases. Irregular emphysema manifests as patchy alveolar destruction with fibrosis, typically occurring in areas of previous lung injury such as infection or scarring.

The pathogenesis of emphysema is driven by a protease-antiprotease imbalance, oxidative stress, and chronic inflammation. Unregulated elastase activity degrades alveolar walls, reducing structural integrity and leading to enlarged air spaces. Oxidative stress induced by cigarette smoke generates free radicals, damaging epithelial cells and weakening pulmonary defense mechanisms. Pro-inflammatory cytokines, including IL–8 and TNF–α, further amplify protease activity and inflammatory damage, accelerating lung injury. The loss of elastic recoil impairs alveolar collapse, resulting in air trapping and lung hyperinflation, which exacerbates gas exchange abnormalities.

Goal

This study aims to investigate the imbalance between proteases and antiproteases in emphysema and its role in extracellular matrix degradation.

Material and methods of research

A retrospective histopathological analysis was conducted on lung tissue samples from 36 patients in the Gomel Region diagnosed with emphysema between 2020 and 2024. Lung biopsy specimens were obtained via transbronchial biopsy and analyzed for alveolar wall integrity, inflammatory infiltration, and fibrosis. Hematoxylin and eosin (H&E) staining was used to assess general tissue architecture, while immunohistochemical analysis measured the expression of elastase, MMP-9, and α1-antitrypsin. Elastin degradation was quantified using Verhoeff-Van Gieson staining, and oxidative stress markers were assessed via immunofluorescence staining.

The results of the research and their discussion

The study involved a total of 36 participants, with ages ranging from 45 to 75 years. The gender distribution was 69% male and 31% female. Regarding smoking history, 75% of the participants were current or former smokers, while 25% were non-smokers.

Histopathological analysis revealed distinct patterns of lung damage. Centriacinar emphysema was the most prevalent subtype, identified in 80,5% of cases, predominantly among smokers. These samples exhibited pronounced destruction of respiratory bronchioles, peribronchiolar inflammation, and moderate fibrosis. Panacinar emphysema was observed in 11,1% of cases, characterized by diffuse alveolar destruction and severe loss of elastic fibers, particularly in α1-antitrypsin-deficient individuals. Paraseptal emphysema was identified in 8,4% of cases, marked by enlarged air spaces adjacent to interlobular septa and bullous changes. Immunohistochemical staining demonstrated significantly increased elastase and MMP–9 expression in severe emphysema cases, correlating with a reduction in α1-antitrypsin levels. Verhoeff-Van Gieson staining confirmed extensive elastin degradation, particularly in panacinar emphysema.

The detailed histopathological findings revealed specific characteristics for each subtype of emphysema. Centriacinar emphysema exhibited an average destruction score of respiratory bronchioles at 7.2 out of 10, a median fibrosis score of 4.5 out of 10, and an average inflammatory cell infiltration score of 6.8 out of 10. Panacinar emphysema showed an average alveolar destruction score of 8.5 out of 10, with severe loss of elastic fibers observed in 85% of cases. Additionally, α1-antitrypsin deficiency was identified in 30% of these cases. Paraseptal emphysema displayed an average enlargement of air spaces at 5.6 out of 10, and bullous changes were present in 25% of cases.

Immunohistochemical analysis provided further insights. Elastase expression levels were measured as 2.3 units per mg of tissue in mild emphysema, 4.7 units per mg in moderate emphysema, and 9.1 units per mg in severe emphysema. MMP–9 expression levels were 1.8 units per mg in mild emphysema, 3.6 units per mg in moderate emphysema, and 7.4 units per mg in severe emphysema. α1-antitrypsin levels were within the normal range of 1.5 to 2.5 units per mg of tissue but were reduced to an average of 0.8 units per mg in severe emphysema cases.

Staining results using the Verhoeff-Van Gieson method revealed elastin degradation scores of 6.2 out of 10 for centriacinar emphysema, 8.9 out of 10 for panacinar emphysema, and 5.1 out of 10 for paraseptal emphysema.

Correlation analysis showed a significant positive correlation between elastase expression and the severity of emphysema ($r=0.78$, $p<0.001$). Conversely, there was a significant negative correlation between α1-antitrypsin levels and the severity of emphysema ($r=0.65$, $p<0.001$).

Conclusions

The comprehensive histopathological and immunohistochemical analysis has provided significant insights into the patterns and mechanisms of lung damage in emphysema. The study confirmed that centriacinar, panacinar, and paraseptal emphysema each have distinct histological features, with varying degrees of destruction, inflammation, and fibrosis. Notably, the severity of elastin degradation and the expression levels of elastase and MMP–9 were positively correlated with the severity of emphysema, indicating their critical roles in the pathogenesis of the disease. Conversely, reduced α1-antitrypsin levels were associated with more severe emphysema, particularly in cases of panacinar emphysema, highlighting the protective role of α1-antitrypsin against elastin degradation.

These findings underscore the importance of considering the subtype-specific characteristics of emphysema in clinical practice and research. They also suggest potential targets for therapeutic interventions, such as modulating elastase activity and enhancing α1-antitrypsin levels, to mitigate lung damage in emphysema. Further research is warranted to explore these avenues and to develop more effective strategies for the prevention and treatment of emphysema.

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