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**Gumeniuk SA, Barkhina TG, Polner SA, Gushchin M.Yu.**

# Clinical, epidemiological and morpho-functional features of bronchial asthma with combined pathology

*To carry out a retrospective analysis of medical records, we have developed an algorithm in which the diagnosis was recorded, reflecting the shape, weight, stage of asthma, sensitization to various groups of allergens, potential comorbidities, gender, age, the main clinical and laboratory parameters received therapy, the timing of finding patient in the hospital. In a retrospective analysis of 1241 case histories of patients were hospitalized in the department of «Asthma» Research Center of the Institute of Immunology Russia for 2007-2011 was found that about 7% (86 people) of the patients with asthma admitted to the hospital with extrahospital pneumonia (EP) . A study of the ultrastructure of the surface of the mucous membranes, and in particular the different populations of cells of the nose and bronchi in the middle and severe asthma when connecting with EP. To study the scanning electron microscopy (SEM) of these divisions sparing methods used world collecting material mucous membranes of the respiratory tract.*

According to official statistics, the number of asthma patients in Russia is about 7 million. However, given the epidemiological data collected in hospitals, the number of asthma sufferers is much lower, at about 3.9 million people, which is the lowest among European countries [1,3]. Of course, these data are significantly understated, in need of correction. This is due to the lack of common approaches to terminology and classification of asthma, as well as standardized methods of diagnosis and treatment of this nosology [2].

Due to the deterioration of the environmental situation in the various regions of our country, an increase in comorbidities was observed in patients with asthma [3]. Among these cases, one should note a frequent combination representing a direct threat to the life of the patient - BA with acute developing outhospital pneumonia (OHP) and the so-called «nocturnal asthma» (NA). Syndrom obstructive sleep apnea (OSA) - a temporary overnight stop respiration, life-threatening and is rarely a cause of sudden death during sleep [5]. Therefore, these combinations of pathologies are dangerous to the lives of patients and cause serious problems during asthma therapy.

When pneumonia is exacerbation of BA, auscultation pneumonic outbreak causes significant difficulties, which generally leads to late diagnosis verification. Please note, that the existing pathology of bronchi and bronchioles, which occur in patients with asthma, pneumonia and pathology joins alveolar and interstitial lung tissue. Therefore, given a combination of two affected all parts of nosology respiratory system, leading to severe intoxication and hypoxia, increases the risk of complications from other systems, causing the need for urgent action intensive care until resuscitation. It should be borne in mind that patients with allergies often changed not only the nature of the reactivity of the bronchi, but also other organs and tissues for any additional exposure that makes significant changes in these complex immunological mechanisms. It should also be noted that previously we noted changes platelets not only in peripheral blood but also in the microvascular of the respiratory and digestive systems in BA. These changes and contributed

to increasing hypoxic and anoxic damage that we observed in patients of asthma [4]. All this has been characteristic motive in the study of clinical and immunological, allergic and morphological aspects of the study group of patients with combined pathology.

Methodology To conduct a retrospective analysis of medical records, we developed an algorithm, in which recorded the sex and age of patients, the diagnosis, reflecting the shape, weight, stage of bronchial asthma (BA); sensitization to various groups of allergens, potential comorbidities, clinical, basic and laboratory data on treatment, time to find a patient in the hospital. In a retrospective analysis of 1241 patients, who were treated at the department of «Bronchial Asthma» Institute of Immunology FMBA of Russia for 2007-2011. We found, that about 7% (86) of the patients with BA admitted to the hospital with OHP. Of the 402 patients studied in 307 people (76.4%) showed signs of obstructive sleep apnea.

For research a map of individual examination of the patient was developed which includes the application form allowing to diagnose of OSA in patients with complaints of snoring and daytime sleepiness. Total for this questionnaire surveyed 402 patients at 76.4% (307 people) found signs of OSA. Mean age 54.2 years. It was found that among these are dominated by patients with a mixed form of asthma 78.0% (288 people) and the medium-severe severity - 73.4% (271 people). Among them were associated pathology 91.8% (369 patients). The majority of patients with OSA obese 77.2% (285), type 2 diabetes, 26.3% (97 people) and hypertensive disease 51.2% (189 people).

Divided into 3 groups of patients: patients with asthma (group 1), patients with OSA without asthma (group 2), and patients with a combination of asthma and OSA (group 3). Control group consisted of healthy male volunteers, whose average age was 35 years.

Methods: physical examination, allergy testing, skin tests, Diagnostics (ERF, test with bronchodilators), polysomnography (PSG), morphological studies of bronchoalveolar lavage (BAL) and peripheral blood cells (scanning and transmission electron microscopy (SEM, TEM).

## OWN RESEARCH AND DISCUSSION

The average age of patients studied (AD and MR) was 42.5 years. The distribution by sex: women accounted for 47 people, men - 39. Experience of the disease was varied and ranged from 1 year to 20 years. The average age of the manifestation of the disease was 12 years. In 50% (43 persons) was burdened by heredity of atopy and 88.4% (38 people) of them on BA. At the same time 34.9% (15) showed a history on the mother, at 7.0% (3 people) on the father, in 58.1% (25 people) through both parents. The emergence of OHP in patients with BA in 88.4% (76) of cases occurred in a cold season. Among the analyzed group, patients were divided according to severity: mild asthma was found in 19% (17 people), medium level - at 55.8% (48 people), and severe degree of asthma - in 24.4% (21 people). Atopic asthma suffered 32.5% (28 people), infection-dependent form 14% (10 people) and a mixed form (atopic and infectious-dependent) - 55.6% (48 people). The average level of total IgE was 306,90 ± 35,1 IU \ ml, which is two times the upper limit of the reference values. When allergology study of patients with atopic asthma without the OHP, atopic asthma with the OHP, mixed with asthma VP spectrum was identified cause-relevant allergens. The results are consistent with a history and results of skin testing. Positive skin prick-tests with different groups of allergens were detected in all patients (Table 1).

In 91.8% (79 people) were observed other manifestations of atopy. Most of the patients suffered from perennial allergic rhinoconjunctivitis at what symptoms have been present for more than 50% of the time, suffering from seasonal allergic rhinoconjunctivitis - 76.7% (66 people), atopic dermatitis - 20.9% (18 people). By analyzing the structure of the co-morbidities of the study group, at

82.5% (71 patients) were mentioned diseases of the upper and lower respiratory tract. So comorbidities ENT (chronic rhinitis of different etiologies, sinusitis, tonsillitis, polypoid rhinosinusopathy etc.) was observed in 40.7% (35 persons), bronchopulmonary pathology (chronic bronchitis, COPD, etc.) - at 59.3 (51 people). Drug intolerance of different drug groups were 50% (43 people), NSAID-transfer 9.3% (4 people), intolerance of different groups of antibiotics (in history) were 21.6% (8). It was also noted that the average age of patients with atopic asthma form lung flow was 31.4 years old, moderate - 44.8 years; severe - these patients have been reported. BA depended- infectious form, easy flow - 36.0 years; moderate - 50.7 years; severe - 72.0 years. Mixed form of asthma, lung flow - 42.5 years; moderate - 47.2 years; severe 61.9 year. The tendency to asthma weighting with age, as well as the transition to a mixed form of atopic form of asthma. As a primary care - was held antibiotic therapy (mostly broad-spectrum antibiotics): one course of antibiotic therapy received 72.0% (62 people), a second course of antibiotics took 28.0% (24 people), and the side effects of use of antibiotic therapy were observed in 24.4% (21 people), they were mostly drugs penicillin group 90.5% (19 patients). SCS received 61.6% of patients (n = 53) of these systemic corticosteroids - 47.6% (41 people). Mucolytics were assigned 84.9% (73 patients), methylxanthines short-acting 41.8% (36 patients), ß2-agonists, short-acting additionally used 13.9% (12 people), berodual 8.1% (7 patients). The mean number of exacerbations per year 3,59 ± 0,45. The mean number of hospitalizations per year 1,51 ± 0,36. Based on analysis of medical records, it was found that quickly started, adequate and simultaneous treatment of both diseases -OHP and asthma, proper selection of rehabilitation therapy helped to reduce the severity of clinical manifestations of the disease in question and the number of complications significantly reduced hospital stay, accelerated period convalescence and recovery efficiency. Cytology of nasal secretions and sputum found mainly coccal flora as well as the presence of a large number of lymphocytes. The study of the nasal mucous membranes by SEM [6] suggests major inflammatory changes of the surface epithelial cells and the build-up to them macrophages and lymphocytes. And the study of BAL revealed serious damage ciliated cells and increased goblet cells, mostly in the extrusion step (fig.1 a,b).

**Table 1. Range of identified allergens.**

| Positive prick-tests with allergens | Group 1 n = 20 | | Group 1 n = 28 | | Group 1 n = 48 | |
|---|---|---|---|---|---|---|
| | the number of persons | % | the number of persons | % | the number of persons | % |
| Dust mites | 12 | 60,0 | 16 | 85,6 | 35 | 72,9 |
| Feather pillows | 3 | 15,0 | 6 | 21,0 | 8 | 16,7 |
| Library dust | 5 | 25,0 | 6 | 21,0 | 10 | 20.8 |
| Hair cats | 8 | 40,0 | 10 | 35,7 | 13 | 27,1 |
| Dog hair | 5 | 25,0 | 5 | 17,8 | 8 | 16,7 |
| Wool sheep | 0 | 0 | 3 | 10,7 | 5 | 10,4 |
| Horse dander | 0 | 0 | 2 | 7,1 | 0 | 0 |
| The family tree | 4 | 20,0 | 6 | 21,0 | 10 | 20,8 |
| The family of grasses | 2 | 10.0 | 5 | 17,8 | 6 | 12,5 |
| The family of weeds | 5 | 25,0 | 10 | 35,7 | 13 | 27,1 |

Group 1 - atopic asthma without the EP. [6] Group 2 - atopic asthma with OHP. Group 3 - mixed BA with OHP.

With the combination of BA with OSA methods were used: a standard physical examination, allergy tests (history taking, questioning of patients, skin scarification tests with atopic allergens, the determination of total and specific Ig-E, on the testimony - nasal provocation tests), Diagnostics (ERF, the sample with bronchodilators), polysomnography (PSG), consulting (ENT, cardiologist, neurologist, endocrinologist (indication)), morphological studies of peripheral blood cells by transmission (TEM) and (SEM).

In functional studies of respiratory (ERF) broncho-pulmonary system in group 3 patients have lower rates of airflow obstruction than in the other two groups, a significant reduction of the flow rate on the bronchi of all calibers.

Poliosomnografiya (PSG) is the preferred method of diagnosis and assessment of severity of OSA [7]. Derived parameters: electroencephalogram, electrooculogram, electromyogram (mentalis), traffic of lower limbs, electrocardiogram, snoring, nasal-oral airflow, respiratory movement of the chest and abdomen, body position, blood oxygen saturation.

Total analysis time averaged 450 minutes, the longest apnea obstruction 60. Apnea index / gipoapnoe (AHI) was 56.6 / h. It should be noted that the PSC has revealed OSA in 35 of 36 patients complaining of respiratory discomfort during the night, which indicates the efficiency of this method and gives us the quality and quantity of sleep efficiency and the level of hypoxia.

Morphologic study of peripheral blood samples by SEM revealed that the greatest changes are observed in 3 patients, a group with a clear increase in the percentage of pathological forms of erythrocytes, which is proportional to depend on the severity of the underlying disease. There was a constant aggregation of red blood cells with a predominance of pathological forms: macrocytes, echinocytes, stomatotsites et al. There was swelling of red blood cells, plasma membrane detachment frequent, with severe gravity - in some cases there is a «shadow» of the complete separation of red blood cells and their membranes. Revealed erythrocytes in comorbidity indicate excessive hemolysis, which is exacerbating the already existing

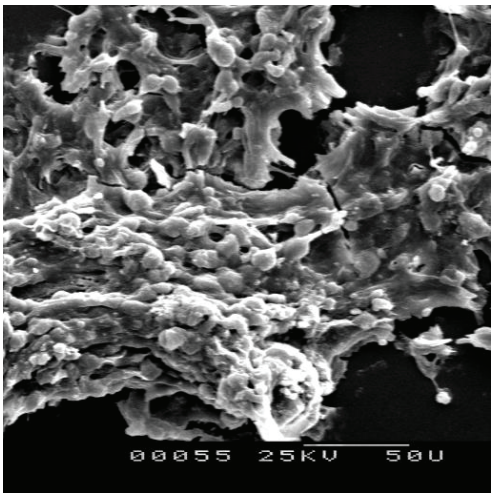


Fig. 1a. SEM. B., 37 years old. BAL. The change in the surface epithelium.
Destruction of ciliated cells (CC). Buildup on their red blood cells, platelets, leukocytes and macrophages. Sharp extrusion of goblet cells (GC) - the desolate cells. Angiogenesis. x 400

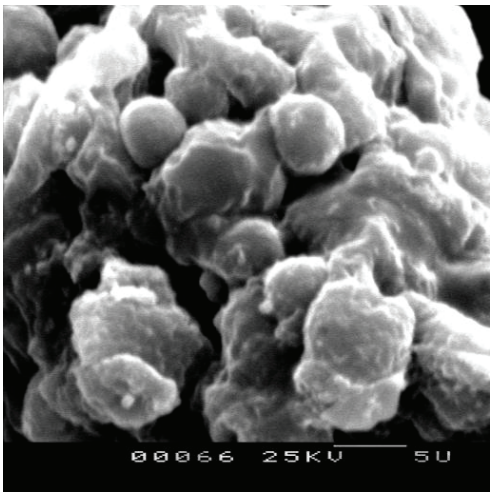


Fig. 1b. SEM. BAL. BC and filled with secret sticking to them macrophages. x 3000.

tissue hypoxia, which generally leads to the development of systemic respiratory failure and not responsive to anti-asthma therapy. Observed in the study of platelet aggregation and accumulation of aggregated groups of platelets, the most pronounced changes were observed in patients 3 groups. Modified forms of platelets differed pretentiousness their shape and pseudopodia, local membrane protrusions and membrane separation from the main cytoplasm. In some parts of the modified form of platelets with numerous spines, had a significant extension and aggregation with others via pseudopodia and directly own platelets.

Therefore, patients with bronchial asthma who have been combined pathology other nosologies deserve special attention of doctors in various specialists.. For these groups of patients need to use a special individual approach aimed at treatment and prevention of BA is not only complex, but also common therapy in general.

**Гуменюк С.А., Бархіна Т.Г., Полнер С.А., Гущин М.Ю.**

**КЛІНІЧНІ, ЕПІДЕМІОЛОГІЧНІ ТА МОРФО-ФУНКЦІОНАЛЬНІ ОСОБЛИВОСТІ БРОНХІАЛЬНУ АСТМУ З ПОЄДНАНОЮ ПАТОЛОГІЄЮ.**

Для проведення ретроспективного аналізу медичної документації нами був розроблений алгоритм, в якому фіксувався діагноз, що відображає форму, ступінь тяжкості, стадію БА, сенсибілізацію до різних груп алергенів, можливі супутні захворювання, стать, вік, основні клініко-лабораторні показники, одержувана терапія, терміни знаходження хворого в стаціонарі. В результаті ретроспективного аналізу 1241 історії хвороби пацієнтів, що знаходилися на стаціонарному лікуванні у відділенні «Бронхіальна астма» Інституту імунології Росії, за 2007-2011 рр. було виявлено, що близько 7% (86 осіб) пацієнтів з БА надійшло у стаціонар з позалікарняною пневмонією (ВП). Проведено дослідження ультраструктури поверхні слизових оболонок, і особливо, різних популяцій клітин носа і бронхів при середньому і важкому перебігу бронхіальної астми при приєднанні пневмонії (ВП). Для вивчення скануючої електронної мікроскопії (СЕМ) цих відділів нами застосовувалися щадні методи збору матеріалу слизових оболонок дихальних шляхів.

*Institute of Human Morphology Moscow, Institute of Immunology, Russia, Moscow*

**Гуменюк С.А., Бархина Т.Г., Полнер С.А., Гущин М.Ю.**

**КЛИНИЧЕСКИЕ, ЭПИДЕМИОЛОГИЧЕСКИЕ И МОРФО-ФУНКЦИОНАЛЬНЫЕ ОСОБЕННОСТИ БРОНХИАЛЬНОЙ АСТМОЙ С СОЧЕТАННОЙ ПАТОЛОГИЕЙ.**

Для проведения ретроспективного анализа медицинской документации нами был разработан алгоритм, в котором фиксировался диагноз, отражающий форму, степень тяжести, стадию БА, сенсибилизацию к различным группам аллергенов, возможные сопутствующие заболевания, пол, возраст, основные клинико-лабораторные показатели, получаемая терапия, сроки нахождения больного в стационаре. В результате ретроспективного анализа 1241 истории болезни пациентов, находившихся на стационарном лечении в отделении «Бронхиальная астма» ГНЦ Института иммунологии ФМБА России, за 2007-2011 гг. было выявлено, что около 7% (86 человек) пациентов с БА поступило в стационар с внебольничной пневмонией (ВП). Проведено исследование ультраструктуры поверхности слизистых оболочек, и в особенности, различных популяций клеток носа и бронхов при среднем и тяжелом течении бронхиальной астмы при присоединении внебольничной пневмонии (ВП). Для изучения сканирующей электронной микроскопии (СЭМ) этих отделов нами применялись щадящие методы сбора материала слизистых оболочек дыхательных путей.

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