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CYTOMORPHOLOGICAL CHANGES IN THE LYMPHOCYTE POPULATION AS AN ADDITIONAL DIFFERENTIAL DIAGNOSTIC CRITERION OF ATYPICAL PNEUMONIA

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Cytomorphological changes in the lymphocyte population were determined to obtain additional criteria for the differential diagnosis of atypical pneumonia and acute respiratory diseases in the first days of illness. The research was conducted among a mobilized individuals and contract military servicemen. Among 84 were patients with acute respiratory diseases, 65 with atypical pneumonia, and 150 conditionally healthy individuals aged 19 to 45 years. The research established differences in cytomorphological changes in the lymphocyte population in atypical pneumonia and acute respiratory diseases in the early days of the illness, reflecting the features of the pathogenesis of these diseases at the immune system level. As additional differential diagnostic criteria for atypical pneumonia and acute respiratory diseases in the early days of illness, the following indicators can be applied: the content of lymphocytes in the form of Botkin-Gumprecht shadows, which is likely higher in acute respiratory diseases.

Key words: atypical pneumonia, acute respiratory diseases, cytomorphology, lymphocytes, population of lymphocytes, pool of lymphocytes, differential diagnostic criteria

О.А. Ракша-Слюсарева, В.І. Трихліб, О.А. Слюсарев, В.І. Задорожна, П.Г. Коваленко ЦИТОМОРФОЛОГІЧНІ ЗМІНИ У ПОПУЛЯЦІЇ ЛІМФОЦИТІВ ЯК ДОДАТКОВИЙ ДИФЕРЕНЦІАЛЬНО-ДІАГНОСТИЧНИЙ КРИТЕРІЙ АТИПОВОЇ ПНЕВМОНІЇ

Для отримання додаткових критеріїв диференціальної діагностики атипової пневмонії та гострих респіраторних захворювань у перші дні хвороби, проведено визначення цитоморфологічних змін популяції лімфоцитів. Дослідження проводились серед контингенту мобілізованих осіб та військовослужбовців за контрактом, серед яких 84 особи були хворі на гострі респіраторні захворювання, 65 осіб хворих на атипову пневмонію і 150 умовно здорових осіб у віці від 19 до 45 років. В результаті досліджень встановлено відмінності цитоморфологічних змін в популяції лімфоцитів при атиповій пневмонії та гострих респіраторних захворюваннях в перші дні захворювання, які віддзеркалюють особливості патогенезу цих захворювань на рівні імунної системи. Як додаткові диференційно-діагностичні критерії атипової пневмонії та гострих респіраторних захворювань у перші дні захворювання, можуть бути застосовані такі показники, як вміст лімфоцитів у вигляді тіней Боткіна-Гумпрехта, вірогідно більший при гострих респіраторних інфекціях, і недостатність імунної системи, яка при атипової пневмонії досягає 100 %, а при гострих респіраторних інфекціях є меншою.

Ключові слова: атипова пневмонія, гострі респіраторні захворювання, цитоморфологія, лімфоцити, популяція лімфоцитів, пул лімфоцитів, диференціально-діагностичні критерії.

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Community-acquired pneumonia, an acute infection of the lung parenchyma acquired outside the hospital, along with other respiratory diseases, causes over 600 million cases of pneumonia and other respiratory illnesses and up to 2.5 million deaths worldwide [4, 7]. In recent decades, atypical pneumonia (AP) has also become significant. The term "atypical pneumonia" emerged in the early 20th century and is closely associated with the description of the classic typical pneumococcal pneumonia, to which it was contrasted. The term "atypical pneumonia" was first used in 1938 by H.A Reimann to describe a pulmonary infection, the clinical characteristics of which differed from those caused by S. pneumoniae. Today, AP is associated with such agents as Chlamydia pneumoniae, Mycoplasma pneumonia, Legionella pneumophila, various viruses, etc. [3, 5, 6]. APs are characterized by subtle clinical features, the absence of typical physical examination findings, and is inadequately diagnosed by modern instrumental methods except for magnetic resonance imaging [2, 3, 5, 10]. Diagnosis and differential diagnosis of AP are especially challenging outside of hospital settings, particularly in the absence of many specialized research methods, such as in military field conditions. Timely diagnosis of AP is crucial for effective treatment, avoiding complications, and preventing chronic disease. Timely diagnosis of AP is crucial for effective treatment, avoiding complications, and preventing chronic disease. Differential diagnosis of AP and acute respiratory diseases in the early days of illness is quite challenging.

Cytomorphological methods, in addition to level I immunological tests, provide the opportunity to simultaneously assess the state and functions of many body systems (nonspecific resistance, the immune

system, the detoxification system, the antioxidant system, the system controlling genetic homeostasis of the body, etc.). Recently, research in this area has resumed, significantly increased, and is being used to determine predictive indicators for various diseases, including in the prognosis and differential diagnosis of pneumonia and other respiratory diseases [8, 9, 11, 12, 13, 14].

Our previous studies using level I immunological methods [2] revealed significant differences in nonspecific resistance indicators between patients with acute respiratory infections (ARI) and atypical pneumonia (AP), which serve as additional criteria for differential diagnosis from ARI in the early days of illness. To complete the development of the differential diagnostic method, it was necessary to determine the cytomorphological changes in the lymphocyte population in AP.

The purpose of the study was to identify probable features and differences of cytomorphological changes in the lymphocytes population in patients with atypical pneumonia for the selection and further development of additional criteria for its early diagnosis.

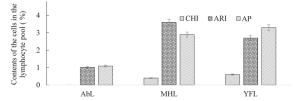
Materials and methods. The blood leukograms of 149 mobilized and contract military personnel who were ill: 84 people with acute respiratory diseases (ARI), 65 people with pneumonia (AP), as well as 150 conditionally healthy people (CHI) aged 19-45 were studied and analyzed. The leukocytes content in peripheral blood and the relative content of peripheral blood leukogram elements were determined using conventional methods [1]. The obtained results were expressed in absolute numbers (G per L) and compared with the normal data for a conditionally healthy population [2]. Frequencies and relative contents within the lymphocyte population were determined for various cell pools: Botkin-Gumprecht shadows (BG), aberrant lymphocytes (AbL), mirror-handle lymphocytes (MHL), spindle-shaped lymphocytes (SSL), young lymphocyte forms (YLF), plasma cells (PC), broad-plasma lymphocytes (BPL), festooned lymphocytes (FL), bean-shaped nucleus cells (BSN), natural killer cell precursors, analogs of natural killer cells - large granular lymphocytes (LGL), Ridder's lymphocytes (RL), dry leaf-shaped nucleus cells (DL), and villous lymphocytes (VL). When analyzing cytomorphological changes of lymphocytes, their quantity per 100 cells of a specific pool was concidered. The obtained results were expressed as percentages (%) and compared with normal data for a conditionally healthy populations. Hidden immune deficiency based on indicators of functionally capable and atypical lymphocytes was determined using the method by O.A. Rakshi-Syusareva et al., (2016). Blood smear preparations were examined using an immersion microscope-trinocular MICROmed XS-4130 at Donetsk National Medical University of the Ministry of Health of Ukraine (Kramatorsk). Statistical analyses utilized the "Statistica Windows" program and a package of corresponding measurement programs.

Results of the study and their discussion. The conducted studies on the frequency of detection of lymphocytes with various cytomorphological changes in patients with AP, ARDS and in CHI showed that their atypical forms, such as pathological villous (VOL) and young spindle-shaped (VL), were not detected in the examined contingents. Pathological cells such as Ridder's cells were not found in patients with AP, but they were registered in 2.0 % of those with ARI.

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(CHI), and in patients with acute respiratory infections (ARI) and

□CHI ⊠ARI ⊠AP

Fig. 1. Content of immature T cells in the lymphocyte population: aberrant lymphocytes (AbL), mirror-handle lymphocytes (MHL), and young functionally capable lymphocytes (YFL) in conditionally healthy individuals (CHI), and in patients with acute respiratory infections (ARI) and atypical pneumonia (AP).

Festooned lymphocytes were found in 30.2±1.2 % of AP cases and 70.1±6.54 % of ARI cases (P<0.05). The frequency of detection of broad-plasma lymphocytes (BPL) was almost the same in patients with AP and ARI, being 57.1±7.0 % and 53±1.7 %, respectively. Plasma cells were significantly more frequently found in AP patients compared to those with ARI, being 42.8±7.0 % and 23.3±1.5 % respectively (P<0.05). Young forms of lymphocytes were significantly more prevalent in AP patients compared to ARI patients, with frequencies of 57.4 ± 7.1 % and 30.2 ± 1.6 % respectively (P<0.05). In contrast, the frequency of immature aberrant lymphocytes was significantly lower in AP (14.2±4.9 %) compared to ARI (30±1.5 %) (P<0.05). Immature T-lymphocytes in the form of mirror-handle lymphocytes were found slightly more frequently in AP than in ARI, being 57.1±1.7 % and 46.6±7.12 %, respectively. Lymphocytes with a beanshaped nucleus were recorded at almost the same frequency in both AP and ARI patients, being 57.1±1.7 % and 60.0±1.7 %, respectively. Large granular lymphocytes were slightly more frequent in AP patients (28.5 %±6.4 %) compared to ARI patients (20±1.4 %). The studies revealed varied differences in cytomorphological changes between AP and ARI patients. Despite all the cytomorphological changes in the lymphocyte pool being atypical or pathological, the frequency of their presence in the peripheral blood of patients in different groups was neither consistent nor significantly different. Therefore, determining the frequency of lymphocytes with specific cytomorphological changes in the peripheral blood of patients cannot serve as a criterion for the differential diagnosis of AP and ARI in the early days of the disease. Consequently, the possibility of determining additional criteria for the differential diagnosis of AP and ARI in the early days of AP and ARI in the early days of the disease. Consequently, of the disease by assessing the relative content of specific pools of cells with cytomorphological changes among the peripheral blood lymphocyte population was considered.

Data on the content of various pools of immature and young cells in the lymphocyte population in patients with acute respiratory syndrome, AP, and CHI are presented in Figures 1, 2, 3, and 4.

The content of the pool of immature T-lymphocytes in the form of aberrant forms (AbL) in the lymphocyte population of patients with AP and ARI showed no significant differences (P<0.05) being 1.9 ± 1.52 % and 1.01 ± 0.4 % respectively. In CHI individuals, Abl was detected. The content of immature T-lymphocytes in the form of a mirror with a handle (MRL) in the lymphocytes population of CHI was 0.4 ± 0.19 % and was significantly lower than in AP and ARI (P<0.05). The content of the MRL pool in AP and ARI was 2.9 ± 0.88 % and 3.62 ± 1.4 %, respectively, and had no significant differences when comparing these groups of patients (P>0.05). The content of functionally capable young lymphocytes (FCL) in patients with AP, ARI, and CHI was 3.3 ± 1.4 %, 2.7 ± 1.34 %, and 1.6 ± 0.2 %, respectively. These indicators had no significant differences (P>0.05). The content of festooned lymphocytes (FL), which are related to the B-cell immunity link, in the CHI group was 0.84 ± 0.22 %, significantly lower (P<0.05) than the indicators in AP and ARI, indicating activation of this link of the immune system in the studied diseases. In patients with AP and ARI, the FL content was 6.0 ± 0.5 % and 6.98 ± 0.97 %, respectively, with no significant differences (P>0.05). The content of plasma cells in AP and ARI was 3.8 ± 0.3 % and 4.7 ± 0.9 %, respectively, and was significantly higher than in CHI (1.3 ± 0.5 %) (P<0.05).

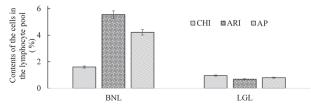


Fig. 3. Content of lymphocyte population precursors of natural killers - cells with a bean-shaped nucleus (BNL), and large granular lymphocytes (LGL) associated with natural killers in conditionally healthy individuals (CHI), in patients with acute respiratory infections (ARI) and atypical pneumonia (AP)

The content of lymphocytes with a beanshaped nucleus (BNL), which are precursors of natural killers, was 1.6 ± 0.3 % in CHI and significantly lower than in AP (4.22 ± 2.07 %) and ARI (5.56 ± 1.57 %) (P>0.05). No significant difference in this indicator was found between AP and ARI patients. The content of large granular lymphocytes (LGL), which are analogs of natural killers, in the examined groups was almost the same: 0.8 ± 0.2 % in AP, 0.68 ± 0.3 % in ARI, and 0.96 ± 0.2 % in CHI.

In patients with AP and ARI, the frequency of detection and content of lymphocyte pools with cells in a state of decay, i.e., Botkin-Gumprecht shadows (B-GS), differed significantly. In AP, the average content of these cells in the lymphocyte pool was 3.69 ± 1.52 %, and in ARI, it was 12.27 ± 4.6 % (P<0.05). Moreover, there was a significant difference in the frequency of registering cell decays in the form of B-GS among the studied groups. B-GS were registered in 71.1 ± 6.47 % of AP patients and 96.6 ± 0.62 % of ARI patients (P<0.05).

Both groups of patients showed immune system deficiency (ISD), both evident (EISD) and hidden (HISD). Data on the evident and hidden immune system deficiency of 1–3 degrees of severity in patients with AP and ARI during examination by first-level immunological methods and the same methods with the addition of cytomorphological studies are presented in Figure 4.

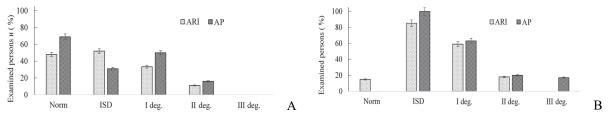


Fig. 4 – Frequency of detection of individuals with normal immune system indicators and immune system deficiency (ISD): overall ISD, ISD I, II, and III degrees in patients with acute respiratory infections and atypical pneumonia in the first (1-3) days of illness when examined using first-level immunological methods (A) and when examined using first-level immunological methods with additional cytomorphological study (B).

As it can be seen from the data presented in Figure 4, the existing immune system deficiency (ISD) was registered based on the indicator of the absolute content of lymphocytes (lymphocyte content less than 1.6 G per litre). ISD was significantly higher in atypical pneumonia (AP) compared to acute respiratory infections (ARI), constituting 66.7 ± 0.96 % and 31.2 ± 3.85 % respectively, with P<0.05. Hidden immune system deficiency (HISD) was recorded as the difference between functionally capable normal forms and

immature and atypical lymphocytes. HISD tended to be inversely related to ISD, amounting to 33.3 ± 7.85 % in AP and 52.3 ± 4.45 % in ARI (P<0.05). Overall, the total immune system deficiency (TISD), which is the combined indicator of ISD and HISD in the first days of illness, was 100.0 ± 0 % in AP and 83.3 % in ARI. However, it is notable that HISD II was much more frequent, and HISD III was exclusively registered in patients with AP. The obtained data also suggest the possibility that the soldiers who fell ill with AP had hidden immune system deficiencies before enlisting in the military.

In addition, our preliminary data [2] indicated changes in the neutrophil (N) and lymphocyte content during atypical pneumonia (AP), with an increase in N as observed by other authors, which is presented as a diagnostic criterion for AP [8, 9, 11, 12]. However, such shifts in leukogram elements are not differentially significant between AP and acute respiratory infections (ARI), as AP can also be caused by viruses [3, 5, 6], which primarily affect lymphocyte counts rather than neutrophil counts. As an additional diagnostic tool for AP and its differential diagnosis from other diseases, many authors [8–14] propose determining the neutrophil-to-lymphocyte ratio (NLR). However, in our studies involving military personnel, this indicator showed significant individual variations (ranging from 6.2 units to 0.81 units), both in cases of AP and ARI. On average, the NLR in AP was 3.6 ± 0.99 units, while in ARI it was 2.5 ± 0.54 units. There were no significant differences observed between NLR in AP and ARI (P>0.05). Similarly, NLR values in AP and ARI did not differ significantly (P>0.05) compared to the average NLR values for physiological norms of 2.47 ± 0.65 units (Speransky II and others, 2009), which reduces the utility of this parameter in the differential diagnosis of AP and ARI.

Thus, the conducted research has demonstrated changes in the relative content of specific lymphocyte pools within their overall population during atypical pneumonia (AP) and acute respiratory infections (ARI). Specifically, compared to ARI, AP showed a tendency towards increased content of young lymphocyte pool cells and a likely decrease in cells associated with B-lymphocytes and plasma cells, despite a significant and likely increase in all these cells compared to healthy individuals (CHI). These immune system changes reflect differences in the pathogenesis of AP and ARI at the level of the immune system, but they cannot be used as predictors of AP. The most likely criterion for the differential diagnosis between AP and ARI is the relative content of lymphocytes in a state of decay, such as Botkin-Gumprecht shadows (TB-G), which are likely more frequently observed in ARI, and the overall (present and hidden) immune deficiency, which reaches 100 % in AP and is lower in ARI.

1. Differences in cytomorphological changes in the lymphocyte population have been identified between atypical pneumonia (AP) and acute respiratory infections (ARI) in the initial days of illness, reflecting differences in the pathogenesis of these diseases at the immune system level.

2. As additional differential diagnostic criteria for atypical pneumonia and acute respiratory infections in the early days of illness, indices such as the content of lymphocytes in the form of Botkin-Gumprecht shadows, which are likely more prevalent in ARI, and the overall immune deficiency, which reaches 100 % in AP and is lower in ARI, can be applied.

Prospects for further research. Development of a method for differential diagnosis of atypical pneumonia and acute respiratory diseases in the early stages of the illness.

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FEATURES OF AXIOGRAMS IN PATIENTS WITH TEMPOROMANDIBULAR DISORDERS AND EXCESSIVE TOOTH WEAR AFTER PROSTHETIC REHABILITATION

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Despite controversial statements about the correlation between temporomandibular disorders and occlusal disorders, most researchers believe that occlusion plays an important role in the etiology of temporomandibular disorders. Excessive tooth wear leads to changes in interdental relationships, insufficient interarch space for restoration or replacement of missing teeth, and positional changes in the mandible. This can result in an increased occlusal vertical dimension after prosthetic treatment, enhancing occlusal load and contributing to symptoms of temporomandibular disorders. In clinical examinations, in addition to the clinical analysis of subjective, objective, and additional methods, the method of electronic axiography with the analysis of functional occlusion in the articulator was employed. A comparative analysis of axiography results in patient groups with increased tooth wear (bruxism) combined with possible other occlusal defects (comparison group) and various forms of temporomandibular disorders: muscular, articulation, combined (main group) before and after occlusal therapy and prosthetic rehabilitation allowed us to establish a significant increase in the quality indicators of axiograms in 78.3 % of patients in the main group out of 37 examined. In the comparison group, the optimal quality of axiogram indicators increased in 83.9 % of patients, compared to 22.6 % before treatment.

Key words: temporomandibular disorders, bruxism, increased tooth wear, axiography, occlusal therapy.

Ю.О. Риберт, Т.І. Пупін, Н.С. Магера, М.А. Дубас, О.Ю. Фецич, Я.О. Семчишин, О.О. Максим ОСОБЛИВОСТІ АКСІОГРАМ ХВОРИХ ЗІ СКРОНЕВО-НИЖНЬОЩЕЛЕПНИМИ РОЗЛАДАМИ ТА НАДМІРНОЮ СТЕРТІСТЮ ЗУБІВ ПІСЛЯ ОРТОПЕДИЧНОЇ РЕАБІЛІТАЦІЇ

Незважаючи на дискусійні твердження про взаємозв'язок скронево-нижньощелепних розладів з розладами оклюзії, більшість дослідників вважають, що оклюзія відіграє важливу роль у сукупності етіологічних чинників розвитку скронево-нижньощелепних розладів. Наявність надмірного стирання зубів, призводить до змін в міжзубному співвідношенні, недостатнього міждугового простору для відновлення або заміни відсутніх зубів, а також спричиняє позиційні зміни нижньої щелепи, що може спричиняти збільшення оклюзійного вертикального розміру після проведеного ортопедичного лікування, посилювати силові навантаження на оклюзійного вертикального розміру після проведеного ортопедичного лікування, посилювати силові навантаження на оклюзійо і сприяти появі симптомів скроневонижньощелепних розладів. У клінічному обстеженні, окрім власне клінічного аналізу суб'єктивних, об'єктивних та додаткових методів, був задіяний метод електронної аксіографії з аналізом функціональної оклюзії в артикуляторі. Порівняльний аналіз результатів аксіографії в групах дослідження хворих з підвищеною стертістю зубів (бруксизмом) у комбінації з можливими іншими оклюзійними дефектами (група порівняння) та різними формами скронево-нижньощелепних розладів: м'язовими, суглобовими, комбінованими (основна група) до та після оклюзіотерапії та ортопедичної реабілітації дозволив встановити достовірне зростання якісних показників аксіограм хворих основної групи у 78,3 % осіб з 37 обстежених, а у хворих групи порівняння оптимальна якість показників аксіограм збільшилася у 83,9 % осіб, проти 22,6 % осіб до лікування.

Ключові слова: скронево-нижньощелепні розлади, бруксизм, підвищена стертість зубів, аксіографія, оклюзійна терапія.

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Temporomandibular disorders (TMD) are a heterogeneous group of conditions affecting the temporomandibular joints (TMJ), masticatory muscles, and associated structures [7, 14]. They have a multifactorial etiology involving systemic, psychosocial, genetic, traumatic, hormonal, neurological factors, and anatomical structure and facial morphology factors [13, 15].

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