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DIAGNOSTIC VALUE OF NON-VIRAL LABORATORY MARKERS OF ACTIVE EPSTEIN–BARR VIRUS INFECTION FOR THE PATIENTS WITH SLE

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The issue of Epstein-Barr virus is the object of research worldwide. It takes an important place in the structure of inflectional diseases. According to the data by World Health Organization, around 90.00-100.00 % of adults are infected with this virus. One of the most important aspects is the study of the virus among the patients with autoimmune diseases including Systemic Lupus Erythematosus since the primary infection with the virus may cause the aggravation of disease or its reactivation may influence on the course of and the symptoms of Systemic Lupus Erythematosus which in its turn may complicate the diagnostics and the disease treatment. Diagnostic value of available non-viral hematological tests has not been enough researched yet.

Material and methods. We have randomly chosen 120 patients by the criterion of Systemic Lupus Erythematosus. Apart from usual tests, the patients were tested for Epstein-Barr virus infections by the way of IgM and IgG antibodies spotting in the blood serum.

Results and discussion. According to the results of general blood test of the patients with Systemic Lupus Erythematosus and active Epstein-Barr virus infection we discovered the reliable connection between the markers, namely: anemia, lymphopenia, monocytosis and accelerated ESR and also the evidence of active Epstein-Barr virus infection. We also discovered a reliable connection between the indices, namely: the increase of the content of creatinine, hyperalaninaminotransferasemia and the increase of hyperaspartataminotransferasemia and the increase of the caption of antistreptolisine О (ASLO), and the evidence of active Epstein-Barr virus infection. Analyzing the changes in proteinogram of the patients with Systemic Lupus Erythematosus, we detected a reliable connection between the markers, namely: the increase of the content of α1– globulins, the decrease of the content of γ-globulins, and the evidence of Epstein-Barr virus infection.

The results of the analysis of the content of circulating immune complexes allowed us to claim that the increase of the caption of average circulating immune complexes are more frequently detected in the patients with active Epstein-Barr virus infection. The obtained results highlighted a reliable connection between the indices, namely: the increase of the caption ANA and the decrease of index of general complement and the evidence of active Epstein-Barr virus infection.

Conclusion. The results of the detection of diagnostic value of the constellations of non-viral laboratory markers of active Epstein-Barr virus infections in the patients with Systemic Lupus Erythematosus did not let us detect peculiar constellations by the sensitivity, specificity and accuracy among them. The evidence of active Epstein-Barr virus infection from the complex of non-viral laboratory markers in the patients with Systemic Lupus Erythematosus is proved by the evidence of hypo α1-globulinemia, or hyperalaninaminotransferasemia, or the increase of the caption of antinuclear antibodies, or the decrease of the indices of general complement, or monocytosis, or the decrease of the content of creatinine, or anemia, or increase ESR, or the decrease of the caption of average circulating immunological complexes, or hypergammaglobulinemia, or hyperaspartataminotransferasemia, or lymphopenia, which may be used in diagnostic algorithm. We did not find particular constellation according to the sensitivity, specificity and accuracy among non-viral laboratory markers of active Epstein-Barr virus infection in the patients with Systemic Lupus Erythematosus.

Keywords: systemic lupus erythematosus, Epstein-Barr virus, diagnostics.

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Introduction. The issue of Epstein-Barr virus (EBV) is the object of research worldwide. It takes an important place in the structure of inflectional...
diseases. According to the data by WHO, around 90.00-100.00 % of adults are infected with this virus [1]. The main reasons for a wide spread of the virus is the capability of whole life persistence after the primary infection with possible periodic reactivation [2].

One of the most important aspects is the study of the virus among the patients with autoimmune diseases including Systemic Lupus Erythematous (SLE) since the primary infection with the virus may cause the aggravation of disease or its reactivation may influence on the course of and the symptoms of SLE which in its turn may complicate the diagnostics and the disease treatment.

In order to spot the active EBV we need to apply expensive serological laboratory tests which are not available in most communal medical institutions of the primary range in our country. Diagnostic value of available non-viral hematological tests has not been enough researched yet.

The purpose of the research was to discover a diagnostic value of non-viral laboratory markers of active Epstein-Barr Virus Infection for among the patients with Systemic Lupus Erythematous.

Material and methods of research. On receiving a written permit to conduct a complex study according to the principles of Helsinki Human Rights Convention, European Board Convention on Human Rights and Biomedicine in accordance with certain laws of Ukraine, we have randomly chosen 120 patients (15 men (12.50 %) and 105 women (87.50 %) at the age from 18 to 69 years old (average age 39.38±12.40 of a year)), by the criterion of with SLE (a complex clinical, laboratory and instrumental examination of all the organs and systems up to the beginning of the treatment according to the orders of the Ministry of Healthcare of Ukraine since 12.10.2006 y. № 676 «On the Confirmation of the Protocols of Medical Care by the Specialty «Rheumatology»). The participants of the research were the patients of the department of Rheumatology of Communal Non-commercial Enterprise of Lviv Regional Council «Lviv Regional Clinical Hospital» in 2013-2016. All enrolled patients signed patient informed consent.

Apart from usual tests, the patients were tested for EBV infections by the way of IgM and IgG antibodies spotting in the blood serum (by the method of immune and ferment analysis according to the instructions). We found out that the infection of the patients with EBV was 99.2 %. Depending on the result of a higher capture of antibodies to EBV, all the patients were divided into two subgroups: 16 patients (13.45 %) with active (higher capture of IgM and the spotting of deoxyribonucleic acid (DNA) of the virus on mouth mucous membrane and / or in the blood serum) EBV infection (research group (RG), out of the list of which were the women at the age from 23 to 69 years old (average age 43.94 ± 3.20 years), and 103 patients (86.55 %) without active EBV (the caption of IgM was within norm) infection (a contrast group (CG)).

The research was conducted in three steps: the first one was dedicated to the analysis of deviations in general blood test, the second step was to determine separate indices of biochemical analysis, the third one was to analyze changes of protein graph in them, the fourth step was to research the content of circulation immune complexes, the fifth one was check the indices of specific immunological research among the patients with SLE RG, CG and the detection depending on their divergent features, and the last one was pointed at the study of constellations of laboratory indices in blood which had the highest indices of specificity, sensitivity and the coefficient of association along with EBV infection and their diagnostics among all the detected deviations.

Statistical analysis was conducted along with the calculation of chances of detecting the phase of infection of EBV of the patients with SLE using a separate feature – the marker which can be detected during a primary medical examination of the patient. A reliable probability of an aggravated phase of infection has been detected with the help of the indices of sensitivity, specificity, accuracy, a chance correlation, an association coefficient (or contingency), a relative risk, an absolute and a relatively lowered risk, a prognostic value of positive result and a prognostic value of negative result [3]. The collected data was processed on the personal computer in MS Excel and SPSS software on the basis of the lists of conjugation with the calculated indices of diagnostic value as well as the software Statistica 6.0 with the use of descriptive statistics and t-criterion by Student (William Silly Gosset) to compare the samples with a normal distribution. We may consider the difference a reliable one when p <0.05, p <0.01 and p <0.001. The connection between active EBV infection and the feature was considered confirmed under the condition of the exceeding by the module of association coefficient 0.5 (or 0.3 for contingency coefficient).

The Results of Research and its Discussion. The Results of the first step of the research have been provided in the table 1.

According to the results of general blood test of the patients with SLE and active EBV infection provided in the table 1, we have discovered the reliable connection between the markers, namely: anemia, lymphopenia, monocytosis and accelerated ESR and also the evidence of active EBV infection. Consequently, we have detected anemia in 14 patients of RG and in 62 patients of CG. The sensitivity of index for the diagnostics of infection amounts to 87.50 %,
Table 1 – Diagnostic Value of Changes in General Blood Test among the Patients with Systemic Lupus Erythematosus with the Active Epstein-Barr Virus Infection (%; sensitivity; specificity; accuracy; correlation of chances; coefficients; risk) depending on the case frequency

<table>
<thead>
<tr>
<th>General Blood Test Indices</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>Chance Correlation</th>
<th>Association Correlation</th>
<th>Contingency Coefficient</th>
<th>Relative Risk</th>
<th>Prognostic Value of Positive Result</th>
<th>Prognostic Value of Negative Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>87.50</td>
<td>39.81</td>
<td>46.22</td>
<td>4.63</td>
<td>0.64</td>
<td>-</td>
<td>3.96</td>
<td>18.42</td>
<td>95.35</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>25.00</td>
<td>79.61</td>
<td>72.27</td>
<td>1.30</td>
<td>0.13</td>
<td>-</td>
<td>1.25</td>
<td>16.00</td>
<td>87.23</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>18.75</td>
<td>85.44</td>
<td>76.47</td>
<td>1.35</td>
<td>0.15</td>
<td>-</td>
<td>1.29</td>
<td>16.67</td>
<td>87.13</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>0.00</td>
<td>93.75</td>
<td>81.08</td>
<td>0.00</td>
<td>-1.00</td>
<td>-0.09</td>
<td>0.00</td>
<td>0.00</td>
<td>85.71</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>13.33</td>
<td>97.50</td>
<td>77.48</td>
<td>0.77</td>
<td>0.04</td>
<td>-</td>
<td>1.07</td>
<td>14.29</td>
<td>86.60</td>
</tr>
<tr>
<td>Lymphocytosis</td>
<td>43.75</td>
<td>80.00</td>
<td>75.00</td>
<td>3.11</td>
<td>0.51</td>
<td>-</td>
<td>2.56</td>
<td>25.93</td>
<td>89.89</td>
</tr>
<tr>
<td>Monocytosis</td>
<td>6.25</td>
<td>85.44</td>
<td>74.79</td>
<td>0.39</td>
<td>-0.44</td>
<td>-</td>
<td>0.43</td>
<td>6.25</td>
<td>85.44</td>
</tr>
<tr>
<td>Acceleration of ESR</td>
<td>43.75</td>
<td>86.41</td>
<td>80.67</td>
<td>4.94</td>
<td>0.66</td>
<td>-</td>
<td>3.63</td>
<td>33.33</td>
<td>90.82</td>
</tr>
</tbody>
</table>

specifcity – 39.81 %, accuracy – 46.22 %. Anemia was detected by 4.63 times more frequently among the patients with active EBV infection than among the patients without active infection. The risk of having active EBV infection was by 3.96 times higher in the case of anemia. We found out a confirmed connection between the marker and belonging to the group with active EBV infection (association coefficient 0.64). Prognostic value of the result, thereby the evidence of aggressive EBV infection in case of anemia amounts to 18.42 %, when its absence in 95.35 % testified to the destitution of active EBV infection.

The decrease of the number of lymphocytes was detected in 7 patients of RG and in 20 patients of CG. Lymphopenia was detected by 3.11 times more frequently among the patients with active EBV infection (the sensitivity of index was 43.75 %, specificity – 80.00 %, accuracy – 75.00 %), than without it. The risk of the rise of active EBV infection was by 2.56 times higher in case of lymphopenia. We have detected a reliable connection between lymphopenia and the belonging to the group with active EBV infection (association coefficient 0.51). The increase of the number of lymphocytes was detected in 1 patient with active EBV infection and in 15 patients without it. The sensitivity of the index for infection diagnostics amounts to 6.25 %, specificity – 85.44 %, accuracy – 74.79 %. We found out unreliable direct connection between the feature and the relation with the group with active EBV infection (association coefficient 0.44). Prognostic value, namely the evidence of active EBV infection in case of lymphopenia amounted to 25.90 %, when it was absent, 89.89 % of patients testified to the absence of active EBV infection.

Monocytosis in 43.75 % of RG patients and in 13.59 % of CG patients. So, the sensitivity of indices for active infection amounted to 43.75 %, specificity – 86.41 %, accuracy – 80.67 %. Monocytosis was by 4.94 times more frequently detected in the patients with active EBV infection than without it. We also detected a reliable connection between the marker and belonging to the group with active EBV infection (association coefficient 0.66). Prognostic value of the result, namely the evidence of active EBV infection in case of monocytosis amounted to 33.33 %, its absence testified to the absence of active EBV infection in 90.82 % of patients.

We found out accelerated ESR in 81.25 % of patients with active EBV infection. Among the patients without active EBV infection accelerated ESR was detected in 53.40 % of patients. Accelerated ESR was detected by 3.78 times more frequently in the patients with active EBV infection than without it. The sensitivity of the index of active infection was 81.25 %, specificity – 46.60 %, accuracy – 51.26 %. We discovered the connection between the marker and the belonging to the group with active EBV infection (direct connection, association coefficient 0.58). Prognostic value of the result, namely the evidence of active EBV infection in case of accelerated ESR amounted to 19.12 %, when its destitution was in 94.12 % and testified to the absence of active EBV infection.

The results of a conducted research allowed us to claim that monocytosis, anemia, accelerated ESR and lymphopenia were most frequently and reliably detected in the patients with SLE and active EBV infection. Similar results described researchers [4] about the connection of anemia, thrombocytopenia and leukopenia in the patients with SLE with active viral infections.

The results of the second step fulfillment of our research concerning the study of separate indices of biochemical blood test is provided in table 2.
The results presented in the table 2 showed a reliable connection between the indices, namely: the increase of the content of creatinine, hyperalaninaminotransferasemia and the increase of hyperaspartaminotransferasemia and the increase of the caption of antistreptolisine O (ASLO), and the evidence of active EBV infection.

As a result, we have detected the increase of the content of creatinine in 2 patients of RG and CG. The sensitivity of the index for diagnostics of active infection amounts to 12.50 %, specificity – 97.06 %, accuracy– 85.60 %. The increase of the content of creatinine was detected by 4.71 times more frequently in the patients with active EBV infection than without it. The risk of having active EBV infection in case of creatinine increase is in 3.23 cases higher. We saw the connection between the increase of the content of creatinine and the belonging to the group with active EBV infection (association coefficient 0.65). Prognostic value of the result, namely the evidence of active EBV infection in case of hyperaspartaminotransferasemia amounted to 3.23 cases higher. We detected a statistically reliable connection between the marker and the dependence on the group with active EBV infection (direct connection, association coefficient 0.70). Prognostic value of the result, namely the evidence of active EBV infection in case of hyperaspartaminotransferasemia amounted to 3.23 times higher. In general, we discovered a confirmed direct connection between hyperaspartaminotransferasemia and dependence on the group with active EBV infection (association coefficient 0.52). Prognostic value of the result, namely the evidence of active EBV infection in case of hyperaspartaminotransferasemia amounted to 27.78 %, the absence – in 89.11 % testifies to the destitution of active EBV infection.

The increase of the content of total cholesterol was detected 64.29 %, specificity – 44.44 %, accuracy – 47.12 %. The increase of the content of creatinine was detected by 4.71 times more frequently in the patients with active EBV infection than without it. The risk of having active EBV infection in case of creatinine increase is in 3.23 cases higher. We saw the connection between the increase of the content of creatinine and the belonging to the group with active EBV infection.

We detected hyperalaninaminotransferasemia in 6 patients of RG and 10 ones of CG. The sensitivity of the indices of diagnostics of active infection amounted to 37.50 %, specificity – 90.29 %, accuracy – 83.19 %. In case of hyperalaninaminotransferasemia the patients had a higher risk of having active EBV infection by 3.86 times. We found out a statistically reliable connection between the marker and the dependence on the group with active EBV infection (direct connection, association coefficient 0.70). Prognostic value of the result, namely the evidence of active EBV infection in case of hyperalaninaminotransferasemia amounted to 37.50 %, absence – in 90.29 % testifies to the destitution of active EBV infection.

The increase of the content of glucose was detected 12.50 %, specificity – 97.06 %, accuracy – 85.60 %. The increase of the content of glucose was detected by 1.70 times more frequently in the patients with active EBV infection than without it. The risk of having active EBV infection in case of glucose increase is in 1.56 cases higher. As a result, we have detected the increase of the content of glucose in 2 patients of RG and CG. The sensitivity of the index for diagnostics of active infection amounts to 12.50 %, specificity – 97.06 %, accuracy – 85.60 %. The increase of the content of glucose was detected by 4.71 times more frequently in the patients with active EBV infection than without it. The risk of having active EBV infection in case of glucose increase is in 3.23 cases higher. We detected the connection between the increase of the content of glucose and the belonging to the group with active EBV infection (association coefficient 0.65). Prognostic value of the result, namely the evidence of active EBV infection in case of glucose increase amounts to 40.00 %, absence – y 87.61 % testified to the destitution of active EBV infections.

Hyperaspartaminotransferasemia was detected in 31.25 % RG patients and in 12.62 % of CG patients. The sensitivity of the indices of diagnostics of active EBV infection amounted to 31.25 %, specificity – 87.38 %, accuracy – 79.83 %. Hyperaspartaminotransferasemia was detected by 3.15 times more often in the patients with active EBV infection than without it. The risk of having active EBV infection in case of hyperaspartaminotransferasemia was by 2.55 times higher. In general, we discovered a confirmed direct connection between hyperaspartaminotransferasemia and dependence on the group with active EBV infection (association coefficient 0.52). Prognostic value of the result, namely the evidence of active EBV infection in case of hyperaspartaminotransferasemia amounted to 27.78 %, the absence – in 89.11 % testifies to the destitution of active EBV infection.
statistically reliable connection between the index and active EBV infection (a confirmed inverted connection, association coefficient -0.85).

According to the obtained data, hyperalanaminotransferasemia, the increase of creatinine content and hyperaspartaminotransferasemia were more often detected in the patients with active EBV infection, when the increase of the caption of ASLO – in the ones without active EBV infection.

The results of our research are similar to the ones of Chinese researchers [5], who described the deviations of the liver functions in the patients with active EBV infection. The researchers [6] also describe the connection of active EBV infection with the rise of autoimmune hepatitis.

The results of the analysis of changes of protein graph in the patients with SLE which has been fulfilled at the third step of our research are provided in table 3.

Analyzing the changes in proteinogram of the patients with SLE, we discovered a reliable connection between the markers, namely: the increase of the content of α₁-globulins, the decrease of the content of γ-globulins, and the evidence of EBV infection.

This way, we discovered 1 patient in RG with the decreased content of α₁-globulins. The same number of patients was discovered in CG. The sensitivity of indices for the diagnostics of active infection amounted to 9.09 %, specificity – 98.73 %, accuracy – 87.78 %. We found out a statistically reliable connection between the indices and the belonging to the group with active EBV infection (the coefficient of contingency 0.77). Prognostic value of the result, namely the evidence of active EBV infection in case of the increase of the content of α₁-globulins amounted to 50.00 %, adestitution – y 88.64 % testified to the absence of active EBV infection.

We detected the increase of the content of γ-globulins in 6 patients of RG and in 21 patients of CG. The sensitivity of the marker amounted to 54.55 % concerning the detection of active infection, specificity – 73.42 %, accuracy – 71.11 %. The increase of the content of γ-globulins was by 3.31 times more frequently detected in the group of patients with active EBV infection. The received results testified to a confirmed direct connection between the increase of content of γ-globulins and the belonging to the group with active EBV infection (association coefficient 0.54).

Prognostic value of the result, namely the evidence of active EBV infection in case of the increase of the content of γ-globulins amounts to 22.22 %, absence – in 92.06 % testified to the destitution of active EBV infection.

The results of the conducted analysis of changes in proteinogram of the patients with SLE allowed us to claim that hypergamaglobulinemia and hypogamma-1-globulinemia are more often detected in the patients with active EBV infection.

The results of the analysis of the content of circulating immune complexes (CIC) during the fourth step of our research is presented in table 4.

We detected the increase of the caption of average CIC in 62.50 % of RG patients. Such changes have been detected in 31.25 % of patients of RG. The sensitivity of the marker was 62.50 % concerning the detection of active infection, specificity – 68.75 %, accuracy – 68.06 %. We confirmed a reliable connection between the marker and the dependence on active EBV infection (association coefficient 0.57). Prognostic value of the result, namely the evidence of active EBV infection in case of the increase of the caption of average CIC amounted to 20.00 %, absence – y 93.62 % testifies to the destitution of active EBV infection.

Table 3 – Diagnostic Value of the Changes in Proteinogram of the Patients with Systemic Lupus Erythematosus with Active Epstein-Barr Virus Infection (%; sensitivity; specificity; accuracy; chances correlation; coefficient; risk) depending on the frequency of cases

<table>
<thead>
<tr>
<th>The Indices of Protein graph</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>Correlation of Chances</th>
<th>Coefficient Association</th>
<th>Coefficient of Contingency</th>
<th>Relative Risk</th>
<th>Prognostic Value of Positive Result</th>
<th>Prognostic Value of Negative Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoproteinemia</td>
<td>0.00</td>
<td>95.60</td>
<td>85.29</td>
<td>0.00</td>
<td>-1</td>
<td>-0.07</td>
<td>0.00</td>
<td>0.00</td>
<td>88.76</td>
</tr>
<tr>
<td>Hypoalbunemia</td>
<td>54.55</td>
<td>53.16</td>
<td>53.33</td>
<td>1.36</td>
<td>0.15</td>
<td>1.31</td>
<td>13.95</td>
<td>89.36</td>
<td></td>
</tr>
<tr>
<td>The Decrease of the Content of α₁-globulins</td>
<td>9.09</td>
<td>98.73</td>
<td>87.78</td>
<td>7.8</td>
<td>0.77</td>
<td>-</td>
<td>4.4</td>
<td>50.00</td>
<td>88.64</td>
</tr>
<tr>
<td>The Increase of the Content of α₂-globulins</td>
<td>18.18</td>
<td>78.48</td>
<td>71.11</td>
<td>0.81</td>
<td>-0.10</td>
<td>-0.83</td>
<td>10.53</td>
<td>87.32</td>
<td></td>
</tr>
<tr>
<td>The Increase of the Content of β-globulins</td>
<td>45.45</td>
<td>70.89</td>
<td>67.78</td>
<td>2.03</td>
<td>0.33</td>
<td>-</td>
<td>1.85</td>
<td>17.86</td>
<td>90.32</td>
</tr>
<tr>
<td>The Increase of the Content of γ-globulins</td>
<td>54.55</td>
<td>73.42</td>
<td>71.11</td>
<td>3.31</td>
<td>0.54</td>
<td>-</td>
<td>2.80</td>
<td>22.22</td>
<td>92.06</td>
</tr>
</tbody>
</table>
The results of a conducted analysis of the caption of CIC in the patients with SLE allowed us to claim that the increase of the caption of average CIC were more frequently detected in the patients with active EBV infection.

The results of the study of specific immunological research in the patients with SLE, conducted at the fifth step of our research, are presented in table 5.

The results presented in table 5 showed a reliable connection between the indices, namely: the increase of the caption ANA and the decrease of index of general complement and the evidence of active EBV infection.

This way, the increase of the caption of ANA was detected in 14 patients of RG and in 69 patients of CG. The sensitivity of the marker amounted to 93.33 % concerning the detection of active infection, specificity – 28.13 %, accuracy – 36.94 %. The received results testified to a confirmed direct connection between the belonging to the group with active EBV infection (association coefficient 0.69).

Prognostic value of the result, namely the evidence of active EBV infection in case of the increase of the caption ANA amounted to 16.87 %, absence – y 96.43 % testified to the destitution of active EBV infection.

There was a decrease of the index of general complement in 87.50 % of patients with active EBV infection and in 58.33 % of patients in the group without infection. The sensitivity of the marker is 87.50 % concerning the detection of active infection, specificity – 41.67 %, accuracy – 50.00 %. The decrease of the indices of general complement was more frequently detected in the patients with active EBV infection than without it. We discovered a confirmed direct connection between the marker and belonging to the

The results of a conducted analysis of the caption of CIC in the patients with SLE allowed us to claim that the increase of the caption of average CIC were more frequently detected in the patients with active EBV infection.

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<table>
<thead>
<tr>
<th>Immunological Indices</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>Chances Correlation</th>
<th>Association Coefficient</th>
<th>Contingency Coefficient</th>
<th>Relative Risk</th>
<th>Prognostic Value of Positive Result</th>
<th>Prognostic Value of Negative Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Increase of the Caption of Big CIC</td>
<td>22.22</td>
<td>64.18</td>
<td>59.21</td>
<td>0.51</td>
<td>-0.32</td>
<td>-</td>
<td>0.55</td>
<td>7.69</td>
<td>86.00</td>
</tr>
<tr>
<td>The Increase of the Caption of Average CIC</td>
<td>62.50</td>
<td>68.75</td>
<td>68.06</td>
<td>3.67</td>
<td>0.57</td>
<td>-</td>
<td>3.13</td>
<td>20.00</td>
<td>93.62</td>
</tr>
<tr>
<td>The Increase of the Caption of Small CIC</td>
<td>100.00</td>
<td>6.25</td>
<td>16.67</td>
<td>-</td>
<td>1.00</td>
<td>0.09</td>
<td>-</td>
<td>11.76</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Table 4 – Diagnostic Value of the Content of Circulation Immune Complexes among the Patients with Systemic Lupus Erythematosus with Active Epstein – Barr Virus Infection (%; sensitivity; specificity; accuracy; chances correlation; coefficients; risk) depending on the frequency of cases

<table>
<thead>
<tr>
<th>Immunological Indices</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
<th>Chances Correlation</th>
<th>Association Coefficient</th>
<th>Contingency Coefficient</th>
<th>Relative Risk</th>
<th>Prognostic Value of Positive Result</th>
<th>Prognostic Value of Negative Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE-cells</td>
<td>43.75</td>
<td>77.67</td>
<td>73.11</td>
<td>2.71</td>
<td>0.46</td>
<td>-</td>
<td>2.31</td>
<td>23.33</td>
<td>89.89</td>
</tr>
<tr>
<td>The Increase of the Caption of Antibodies to double stranded DNA (anti- dsDNA)</td>
<td>100.00</td>
<td>19.80</td>
<td>30.77</td>
<td>-</td>
<td>1.00</td>
<td>0.18</td>
<td>-</td>
<td>16.49</td>
<td>100.00</td>
</tr>
<tr>
<td>The Increase of the Caption of antinuclear antibodies (ANA)</td>
<td>93.33</td>
<td>28.13</td>
<td>36.94</td>
<td>5.48</td>
<td>0.69</td>
<td>-</td>
<td>4.72</td>
<td>16.87</td>
<td>96.43</td>
</tr>
<tr>
<td>The Increase of the Caption of Antiphospholipide Antibodies of IgM</td>
<td>12.50</td>
<td>65.31</td>
<td>70.21</td>
<td>0.65</td>
<td>-0.21</td>
<td>-</td>
<td>0.69</td>
<td>12.50</td>
<td>82.05</td>
</tr>
<tr>
<td>The Increase of the Caption of Antiphospholipide Antibodies of IgG</td>
<td>25.00</td>
<td>82.50</td>
<td>72.92</td>
<td>1.57</td>
<td>0.22</td>
<td>-</td>
<td>1.44</td>
<td>22.22</td>
<td>84.62</td>
</tr>
<tr>
<td>The Decrease of the Indices of General Complement</td>
<td>87.50</td>
<td>41.67</td>
<td>50.00</td>
<td>5.00</td>
<td>0.67</td>
<td>-</td>
<td>4.00</td>
<td>25.00</td>
<td>93.75</td>
</tr>
</tbody>
</table>
group with active EBV infection (association coefficient 0.67).

The results of the analysis of specific immunological research allowed us to claim that the increase of the caption ANA and the decrease of the index of general complement were more frequently detected in the patients with SLE with active EBV infection.

The results of the detection of diagnostic value of the constellations of non-viral laboratory markers of active EBV infections in the patients with SLE (the sixth step), among which there was a general blood test, proteinogram, biochemical analysis, the determination of circulating immune complexes, specific immunological research did not let us detect peculiar constellations by the sensitivity, specificity and accuracy among them.

Conclusion. The evidence of active Epstein-Barr virus infection from the complex of non-viral laboratory markers in the patients with Systemic Lupus Erythematosus was proved by the evidence of hypogammaglobulinemia — (association coefficient 0.77), or hyperalanaminotransferasemia (0.70), or the increase of the caption of antinuclear antibodies (0.69), or the decrease of the indices of general complement (0.67), or monocyotosis (0.66), or the decrease of the content of creatinine (0.65), or anemia (0.64), or increase of ESR (0.58), or the decrease of the caption of average circulating immunological complexes (0.57), or hypergammaglobulinemia (0.54), or hyperaspartataminotransferasemia (0.52), or lymphopenia (0.51), which may be used in diagnostic algorithm.

We did not discover particular constellation according to the sensitivity, specificity and accuracy among non-viral laboratory markers of active Epstein-Barr virus infection in the patients with Systemic Lupus Erythematosus.

Prospects of further researches is the studying of the influence of active Epstein-Barr viral infection for disease activity in patients with systemic lupus erythematosus.

References

Резюме
Рамос-Касалс М, Курдрад М. І., Альба П., Санна Г., Брито-Зерон П., Бертолачини Л. і інші. Агостииальний інфекції в хворих з системним лупусом. Бюлетень внутрішніх захворювань, 2018; 57(11): 811-5.

Абрагамович У. О., Абрагамович О. О., Гута С. І., Циганік Л. В., Романюк О. Т. Резюме. У своєму світі активно вивчається проблема вірусу М. Е. Єпштейна - І. Барр, який займає важливе місце в структурі інфекційних хвороб. Згідно матеріалам Всесвітньої організації охорони здоров’я, близько 90,00-100.0 % дорослого населення інфіковані цим вірусом. Особливо важливим є вивчення впливу вірусу у хворих системним червоним вовчаком, оскільки первинне інфікування вірусом може сприяти загостренню хвороби, або ж його реактивація може вплинути на перебіг та прояв системного червоного вовчака, а це, в свою чергу, може ускладнювати діагностику та лікування недуги. Діагностична цінність доступних невірусологічних гематологічних досліджень вивчена недостатньо. У рандомізованому спосібі із попередньою стратифікацією за наявністю системного червоного вовчака у дослідженні запущено 120 хворих. Окрім рутинних обстежень, пацієнтам проводилось визначення інфекції вірусу М. Е. Єпштейна - І. Барр шляхом виявлення антитіл IgM та IgG до вірусу у сироватці крові. Як свідчать результати дослідження загального аналізу крові у хворих на системний червоний вовчак із активною інфекцією вірусу М. Е. Єпштейна - І. Барр, виявлено достовірний зв’язок між маркером, а саме: анемією, лімфопенією, моноцитозом та присвіренням ШОЕ, та наявністю активної інфекції вірусу М. Е. Єпштейна - І. Барр. Аналізуючи результатів показників біохімічного аналізу крові, нами виявлено достовірний зв’язок між показником, а саме: збільшенням вмісту креатиніну, гіпераланінамінотрансфераземії, гіпераспартатамінотрансфераземії та збільшенням титру антистрептолізину О (АСЛО), та наявністю активної інфекції вірусу
М. Е. Епштейна - I. Барр. Також виявлено достовірний зв'язок між маркерами, а саме: зменшення вмісту α1-глобулінів, збільшення вмісту γ-глобулінів, та наявністю активації інфекції вірусу М. Е. Епштейна - I. Барр. Збільшення титру середніх ЦЖК, збільшення титру ANA і зменшення показника загального компоненту частіше виявляється у хворих із активною інфекцією вірусу М. Е. Епштейна - I. Барр. Про наявність у хворих на системний червоний вовчак активної інфекції вірусу М. Е. Епштейна - I. Барр з комплексу невірусологічних маркерів достовірно частіше свідчить наявність γ-глобулінів, або гіпераланинамінотрансфераземії, або збільшення титру антінуклеарних антител, або зменшення показника загального компоненту, або моноцитозу, або збільшення вмісту креатиніну, або анемії, або прискорення швидкості осадження еритроцитів, або збільшення титру середніх циркулюючих імунних комплексів, або гіпергамглобулінів, або гіпераспартамінотрансфераземії, або лімфопенії, що може бути використано в діагностичному алгоритмі. Характерних констеляцій за чутливістю, специфічністю та точністю серед невірусологічних маркерів активної інфекції вірусу М. Е. Епштейна - I. Барр у хворих на системний червоний вовчак не виявлено.

Ключові слова: системний червоний вовчак, М. Е. Епштейна - I. Барр вірус, діагностика.

УДК 616.5-002.525.2; 616.988.55-07
ДИАГНОСТИЧЕСКАЯ ЦЕННОСТЬ НЕВИРУСОЛОГИЧЕСКИХ ЛАБОРАТОРНЫХ МАРКЕРОВ АКТИВНОЙ М. Е. ЭПШТЕЙНА-И. БАРР ВИРУСНОЙ ИНФЕКЦИИ У БОЛЬНЫХ СИСТЕМНОЙ КРАСНОЙ ВОЛЧАНКОЙ

Абрагамович У. О., Абрагамович О. О., Гута С. И., Цицанник Л. В., Романюк О. Т.

Резюме. Во всем мире активно изучается вирус М. Е. Эпштейна - И. Барр, который занимает важное место в структуре инфекционных болезней. Согласно материалам Всемирной организации здоровья, около 90,0-100,0% взрослого населения инфицированы этим вирусом. Особенно важным является изучение влияния вируса на больных системной красной волчанкой, поскольку первичное инфицирование вирусом может способствовать обострению болезни, или его реактивация может повлиять на ход и проявления системной красной волчанки, а это, в свою очередь, может затруднить диагностику и лечение болезни. Диагностическая ценность доступных невирусологических гематологических исследований изучена недостаточно. В рандомизированное способ с предыдущей стратификации при наличии системной красной волчанки в исследование привлечено 120 больных. Кроме рутинных обследований, пациентам проводилось определение инфекции вируса М. Е. Эпштейна-И. Барр путем выявления антигена вируса у больных системной красной волчанкой. Как свидетельствуют результаты исследования общего анализа крови у больных системной красной волчанкой с активной инфекцией вируса М. Е. Эпштейна-И. Барр, обнаружено достоверная связь между маркером, а именно: анемией, лимфопенией, моноцитозом и ускорением СОЭ, и наличием активной инфекции вируса М. Е. Эпштейна-И. Барр. Анализируя результатов показателей биохимического анализа крови, нами обнаружено достоверная связь между показателем, а именно: увеличением содержания креатинина, гипераланинаминотрансфераземии, гипераспартаминотрансфераземии, гипергамглобулинемии, креатининемии, содержания креатинина, гипергамглобулініемії, креатінініемії, гіпераспартатамінотрансфераземії, або гіпераспартатамінотрансфераземії, або лімфопенії, що може бути використано в діагностичному алгоритмі. Характерних констеляций за чутливістю, специфічністю та точністю серед невірусологічних маркерів активної інфекції вірусу М. Е. Эпштейна - И. Барр у больных системной красной волчанкой не обнаружено.

Ключевые слова: системная красная волчанка, М. Е. Эпштейна - И. Барр вирус, диагностика.

The authors of this study confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of coauthors of the article.

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