

Clinical Research

Some Indicators of Antibody-Independent Effector Mechanisms in Latent Sero-Resistant Forms of Syphilis

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Abstract

Currently, there is an alarming increase in the syphilis rates accompanied by a proportional rise in the incidence of latent forms of the disease among the population of several countries. Latent syphilis considerably delays timely detection, diagnosis and, therefore, the specific early treatment of patients. In 2007, the proportion of latent forms of syphilis in the Russian Federation amounted to 49.7% of all reported syphilis cases [6]. Importantly, it is very important to note latent syphilis was found in each of the 4 cases of HIV-infected patients. [7]. The absence of clinical manifestations in patients with this type of syphilis is of great scientific and practical interest, and only serological examination is seen to contribute to the diagnosis of this disease. The properties of the *Treponema pallidum* (TP) and the state of immunity in the infected person are well known to be the main factors influencing the development of the pathology. However, studying the properties of the causative agent of syphilis is quite impossible because modern strains of TP are absent. In this connection, the relevance of studying the characteristics of protective mechanisms in the latent forms of syphilis is obvious. In our study, we investigated the amount of T-lymphocytes and their subpopulations, which are CD2, CD3, CD4, CD8, CD16, CD19 and CD25. The study identified a significant deficiency of CD4⁺ and suppressive/cytotoxic T cells, as well as significantly low levels of CD25, which is important in stimulating the proliferation of T and NK cells. IJBM 2012; 2(1):38-40. © 2012 International Medical Research and Development Corporation. All rights reserved.

Key words: latent syphilis, sero-resistance, T-lymphocytes.

Introduction

In recent years, the incidence of the latent forms of syphilis has increased due to the widespread increase of the disease. Early latent syphilis has now risen to 60-96% of all the cases of latent disease, and it is registered significantly more often than late syphilis and unspecified [6]. One of the determining factors of the development of syphilis in humans is the condition of his immune system.

In particular, the antibody-independent effector mechanism plays a very important role and their study has acquired enormous interest in understanding the protective mechanisms in the genesis of syphilis, particularly the latent and sero-resistant forms. The urgency of studying the defense mechanisms of this disease is emphasized by the significant increase in the number of syphilis patients with HIV, in recent years [7]. The development of the immune response with the mandatory participation of T and B cells begins after penetration of TP through the skin and mucous barriers into the internal environment of the human organism. During this period, the non-specific cellular mechanisms begin to act and pass the baton to the lymphocytes, which provide greater protection from infection than phagocytosis. The subpopulation of T and B cells memorize the causative agent and trigger a heightened immune response to it on the re-entry of the

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disease agent [2, 6].

Purpose

To study the blood level of the T-lymphocytes and their subpopulations which include CD2, CD3, CD4, CD8, CD16, CD19, CD25 and HLA-DR that are involved in the formation of specific immunologic reactivity in the latent forms of syphilis.

Material and Methods

Blood samples of 20 patients (12 men and 8 women) with latent sero-resistant forms of syphilis were examined. However, patients were not divided according to the period of the disease. The median age was 35.3 years (V_{\min} -20, V_{\max} -42). Flow cytometry and immunocytofluorimetry methods were used on "CYTOMICS FC 500" (Beckman Coulter, USA) to determine the lymphocyte subpopulations. Statistical data and analysis of the results were done on a personal computer using the BIOSTAT software. Then, parametric and nonparametric methods were used in accordance with the generally accepted provisions [2, 4]. On analysis, the

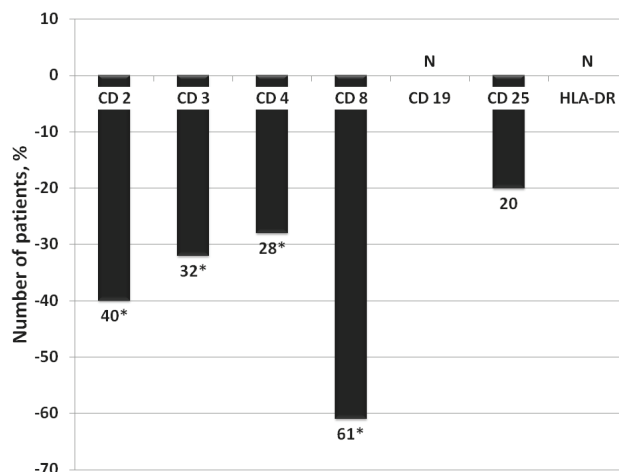
distribution of the variable calculated frequencies of individual values, mean, standard error of the mean, student's t test, confidence level, and the level of significance p was deduced. The significance level was assumed to be equal 0.05, which ensured a reliability of >95% ($p < 0.05$). We used the Pearson's correlation coefficient, as well as the match criterion Pearson - chi-square (χ^2). The relationship between the two variables was measured based on Kramer's coefficient [1].

Results

Analysis of the data revealed a reduced blood lymphocyte level with the antigenic markers of CD-8 in 61%. Low levels of lymphocytes with CD2, CD3, CD4 antigenic markers were detected in 40%, 32% and 28%, respectively (Fig.1). The relative number of CD19 lymphocytes did not differ from normative values. Blood levels of the activation markers CD25 and HLA-DR were also found to be within normal limits. In calculating the absolute number of lymphocytes a reduction in the levels of CD3 - lymphocytes was noted in 44% patients, CD19 - in 40% of patients, and early activation marker CD25 in 100% of the patients (Fig.2).

Figure 1.

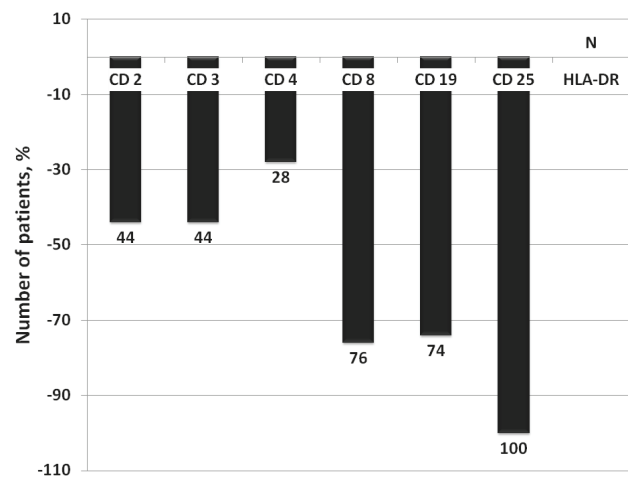
Distribution of patients with latent sero-resistant syphilis, with relative immunological parameters outside of the physiological abnormalities.



Note: * - $p < 0.05$

Figure 2.

Distribution of patients with latent sero-resistant syphilis, with absolute immunological parameters outside of the physiological abnormalities.



Discussion

Our analysis, done using the nonparametric method, specifically, the Pearson's criteria, revealed a significant decrease in almost of all the investigated subpopulations of lymphocytes in the blood of patients with latent and sero-resistant forms of syphilis. This occurred because of a relative increase in the number of patients with decreased values of lymphocyte subpopulations below the minimum

limit in healthy people. In the analysis, we included a provision stating that the ratios of the indicators, but not their absolute values, are of significant and paramount practical concern in assessing the immunogram [2-4]. Also, the increase in the percentage of cells without changing their absolute number was considered to be possibly associated with their migration from the central and peripheral organs of the immune system in the area of the pathological focus. However, other researchers believe

that the absolute values more clearly demonstrate the potential of lowering the immune system because, in addition, they reflect age-related changes in the number of lymphocytes [4, 8]. In this connection, attention was drawn to a significant decrease in the level of the early activation marker SD25, which provided the formation of a high-affinity receptor on the cell surface for IL-2, the main biological effect of which is to stimulate the proliferation of T and NK cells. Interestingly, activation using markers SD25 is known to extend to the B cells (CD19) as well [5].

Conclusion

Thus, our results prove that patients with the latent sero-resistant forms of syphilis are characterized by the presence of a significant immunodeficiency of the T-helper lymphocytes (CD4) and suppressor/cytotoxic T cells. Perhaps these changes are the result of reducing the CD2-dependent activation of alternative T lymphocytes, due to the significant decrease in the CD2-lymphocytes in 44% patients. Also, the presence of the significantly low levels of the early activation marker CD25 was identified, which is involved in stimulating the proliferation of the T and NK cells. All the above mentioned stages indicate the inhibition of activation processes directed toward the proliferation of cellular elements with their subsequent differentiation in the effector cells, and this has a certain important bearing on the formation of the latent form of syphilis.

References

1. Zaitsev VM, Lifyandsky VG, Marinkin VI. Applied Medical Statistics. St. Petersburg, 2003.
2. Levashova TV. Method for determination of minor subpopulations of T-lymphocytes with alpha/beta and gamma/delta T-cell receptor. Abstracts of the Ninth All-Russian Medical and Biological Conference of Young Researchers "Man and his health", 22 April 2006; 93-96.
3. Levashova TV, Miroshnichenko IV. Double-negative T-cells in diseases associated with inflammation. Abstracts of the II All-Russian Scientific-Practical Conference "Society, State, and medicine for the elderly and persons with disabilities", September 2005; 62-63.
4. Sergeenko VI, Bondarev IB. Mathematical statistics in clinical trials. Moscow: GEOTAR-Media, 2006. p. 186-194.
5. Khaitov RM. Immunology. Moscow: GEOTAR-Media, 2006.
6. Chebotarev VV. Syphilis. Stavropol, 2010.
7. Chereshev VA., Patrusheva NB, Beykin Ya.B. et al. Syphilis: the immune system and laboratory diagnosis. Yekaterinburg: Ural Branch of RAS, 2006. p. 25-81.
8. Cherinikh TV, Kashkin SV, Zaitseva GA, Mamaeva TA. Character immunological changes in patients with syphilis with severe clinical manifestations. Abstracts of the 3rd All-Russian Congress of Dermato-venereology. Kazan, 2009; S.97.