

Significance of Immunological Indexes in Prognosis Assessment of Influenza

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Abstract

Influenza viruses cause serious infections in millions of people every year due to their high mutagenicity, which imposes a great burden on social, economic and medical resources. Different subtypes of influenza virus infection have different effects on human immune system, which are reflected in different changes in lymphocyte and cytokine levels. Therefore, we can learn how the immune system is responding to the flu virus through taking blood samples from patients and testing them. This article reviews some recent studies in this field, and summarizes some valuable conclusions, in order to provide a reference for clinical treatment.

Keywords

Influenza A; Lymphocytes; Cytokines; Indicators of Disease Assessment.

1. Introduction

Influenza virus infection has become a major public health concern since the last century, causing millions of severe cases and hundreds of thousands of deaths worldwide each year. They are classified according to the type of hemagglutinin and neuraminidase on their surface. Of these, the ones that have the greatest impact on humans are A (H1N1) virus. Because influenza viruses are highly susceptible to genetic drift and mutation, new strains are constantly emerging to infect humans, and even viruses that previously infected birds (such as H7N9) are circulating in humans. In the process of resisting influenza virus infection, human lymphocytes and cytokines play an important role, and the levels of various lymphocytes and cytokines maintain a dynamic change during the course of infection. Some of these values can be used as indicators to assess the patient's condition and provide a reference for treatment. Recent studies have shown that in severe patients with influenza virus infection, many cytokines are secreted in large quantities, which together with lymphocytes produce adverse consequences, such as alveolar membrane edema, a phenomenon known as "cytokine storm". In recent years, there have been a lot of studies on lymphocytes and cytokines of influenza patients as well as the evaluation criteria of the disease, most of which adopt the method of analyzing blood cells or serum of patients, but there is still a lack of systematic discussion on the results of these studies. Therefore, this review will review the research in this field, with a focus on lymphocytes and cytokines closely related to "cytokine storm", with a view to providing ideas for further research and intervention of this immunological phenomenon that seriously harms critically ill patients.

2. Immune response to influenza a virus infection

2.1. Lymphocyte changes

At present, most of the research on the change of lymphocyte level after influenza A (H1N1) virus infection focuses on CD3⁺, CD4⁺ And CD8⁺T cells. Most studies have shown that the number of these three types of T cells in the blood of influenza A patients is reduced to varying degrees compared with that of healthy people. But there are also some studies that show CD8 in some

A (H1N1) patients' T cells increased (42.27 ± 11.13) cells/ μ l at the initial stage of diagnosis, but returned to normal (29.26 ± 12.99) cells/ μ l at the recovery stage. [1]. By contrast, in patients with mild disease, the study data in patients with severe disease and death of influenza can be found that with the development of the severity of the disease, the T cell counts of all types of patients have further decreased. For convalescent patients, the T cell count of all types increased to varying degrees [2]. CD3 has been reported in pediatric patients' T cells, CD4⁺ T cells and CD8⁺ T cell levels were all decreased, including CD4⁺ T cells are better than CD8⁺ T cells. The T-cells went down even more [3]. CD4⁺% and CD4⁺/CD8⁺ also decreased with the increase of disease severity. The T-cell count of mild patients returned to normal three days after diagnosis, and that of critically ill patients began to decline three days after diagnosis. After the virus turned negative, the T-cell count returned to the base level but did not return to normal [4]. But for CD4⁺/CD8⁺ However, some researchers found no significant difference between critically ill patients, critically ill patients and those who died [2]. In addition to the above three types of T cells, changes in the levels of specific types of CD160⁺ CD8⁺ T cells, such as the initial T cell (T_N), central memory T cells (T_{CM}), effector memory T cells (T_{EM}), terminal effector memory T cells (T_{EMRA}) were significantly reduced in influenza A virus infected patients, have also been reported Programmed cell death factor 5 (PDCD5) is a pro-apoptotic factor, which can promote apoptosis and inhibit proliferation of many kinds of cells. The B lymphocytoma-2 gene (Bcl-2) is a proto-oncogene involved in apoptosis. The above changes in T lymphocytes may be attributed to the high expression of PDCD5 and low expression of Bcl-2 in peripheral blood of the patients, with a significant negative correlation between the two. The apoptosis of T lymphocytes may be related to the expression of PDCD5 and Bcl-2. Peripheral blood CD3 in patients with influenza pneumonia' T cells and CD3⁺ CD4⁺ T cell subsets and CD3⁺ CD8⁺ The apoptotic ratio of T cell subsets was significantly higher than that of healthy controls, including CD3⁺ CD4⁺ The apoptosis of T cell subsets was more significant, which was positively correlated with the expression of PDCD5 and negatively correlated with the expression of Bcl-2. However, studies have shown that the positive expression rate and expression level of Bcl-2 in the peripheral blood of patients with influenza pneumonia are lower than those of healthy control group, and the expression of PDCD5 and Bcl-2 is negatively correlated. So that tells us that CD3⁺ T cells and CD3⁺ CD4⁺ T cell subsets and CD3⁺ CD8⁺ Apoptosis of T cell subsets is associated with the pathogenesis of influenza pneumonia [5].

2.2. Changes in cytokines

Because of many infectious diseases in severe cases, the "cytokine storm" will be the phenomenon, so for the a/h1N1 flu patients cytokine levels change research has focused on closely related to "cytokine storm" some cytokines, such as interleukin (IL) and interferon (IFN), tumor necrosis factor (TNF), etc. The essence of cytokine storm is the intense inflammatory storm caused by the release of a large number of pro-inflammatory cytokines. The known pro-inflammatory cytokines mainly include IL-6, IL-8, IL-17, IL-18, TNF- α , etc. In patients infected with influenza A (H1N1) virus, we noticed significantly higher levels of IL-6 and IL-10 in patients compared to healthy people [6] The levels of TNF- α and MCP-1 (monocyte chemotaxis protein) were also increased in different degrees, which are related to the occurrence and development of atherosclerosis. Therefore, it is suggested that influenza A virus infection may be associated with the occurrence of atherosclerosis. The levels of IL-2, IL-6, TNF- α and IFN- γ were significantly higher in severe and mild patients [6].

Many cytokines in the cytokine storm have their different functions. Type I and III IFN protect the host against influenza virus infection by promoting virus clearance and antiviral immune response. TNF- α is the central proinflammatory cytokine of the influenza cytokine storm, and its elevated level indicates the higher pathogenicity of the virus, indicating the possibility of further aggravation of symptoms after infection. IL-6 activity is reduced during secondary

bacterial infection, which may facilitate the clearance of the virus from the body and have a beneficial effect on patient survival. Important cytokines secreted by Th1 cells include IFN- γ , and important cytokines secreted by Th2 cells include IL-10. The role of the former is to protect the body in the process of infection, such as promoting the elimination of virus, inducing immune response, etc. The latter is a representative anti-inflammatory cytokine. Studies have shown that IL-10 is highly expressed in influenza patients, and its level is positively correlated with the severity of pulmonary inflammation.

In children, compared with healthy control group, serum total NO, NO₂⁻, IL-17, IL-2, TNF- α , IL-6, IL-10 levels were significantly increased in children with A H1N1, while IL-4 was significantly lower than that in control group, and IFN- γ levels were decreased, but there was NO statistical difference. Due to the disorder of the immune system in children with A (H1N1), the large release of pro-inflammatory factors, the enhancement of oxidative stress such as nitric oxide and the decrease of immune function of T cells are not conducive to the timely clearance of pathogens [7].

3. Conclusion

Influenza virus is a pathogen that seriously threatens human health. Many scholars have studied and proposed its influence on human immune system. The concept of "cytokine storm" has further deepened our cognition of severe influenza. In terms of lymphocyte changes, with the increase of the severity of the disease in general, T lymphocytes show a decreasing trend, especially CD4, which plays an immune role. And CD8⁺T cells, which may be due to the increased level of IL-10 in the patient, because IL-10 has a strong immunosuppressive effect and can inhibit lymphocyte proliferation. In terms of cytokine changes, in view of the "cytokine storm" research has shown that cytokine TNF alpha is center, the cytokine storm and disease progression in patients with plays an important role in the process, so the TNF alpha and the IL - 10 May become the new targets for therapy for severe influenza especially flu, these two kinds of cytokines single resistance is likely to replace the present stage IFN therapy in clinical practice but the effect not beautiful. An important significance of exploring the changes of lymphocyte and cytokine levels in patients is to provide reliable quantitative indicators for evaluating patients' conditions. According to statistical analysis, the elevation of NLR (neutrophils/ lymphocytes) indicates that the patient's disease is more serious and the prognosis is poor, and some studies have found that ΔNLR_3 (NLR of three days of hospitalization -- NLR of the day of admission) can be used as an independent predictor of mortality risk. Based on these research results, some scholars have proposed new possible methods to treat influenza from the perspective of direct regulation of immune response. For example, IL-37, a newly discovered member of the IL-1 family, has strong anti-inflammatory properties and may be useful in treating patients with severe illness caused by the H1N1 virus [8]. From the abnormal changes of lymphocytes and cytokines in the body at the time of infection with influenza virus described in this paper, we may also find more effective drugs and methods against influenza virus.

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