# The Value of Lymphocyte Subsets and Cytokines in Adult Minimally Change Disease

# Xiaomeng Zheng, Lin Duan<sup>\*</sup>, Chengbi Tong, Xiaodong Li, Xiaodan Liu

Department of Clinical Laboratory, Afliated Hospital of Hebei University, Baoding, 071000, China \*Corresponding author

Keywords: Adult Minimal Change Disease; Lymphocyte Subsets; Cytokines

Abstract: Adult Minimal Change Disease (AMCD) is a common autoimmune disease, which is characterized by glomerular basement membrane injury, proteinuria, hematuria, and hypertension. Researchers have found that at present, the pathogenesis of AMCD is still unclear, and there is no effective treatment, so studying the pathogenesis and treatment of AMCD holds great practical significance. This paper mainly discusses the role of lymphocyte subsets and cytokines in AMCD, and the relationship and regulation between them. Firstly, the text expounds the importance of lymphocyte subsets and cytokines from the pathogenesis, disease development, and treatment response of AMCD. Then, it emphasizes the significance of the interaction and synergy between lymphocyte subsets and cytokines in AMCD, and the authors put forward a new strategy of targeted therapy for lymphocyte subsets and cytokines. Through an in-depth understanding of lymphocyte subsets, cytokines, and their relationship in AMCD, researchers can more clearly understand the pathogenesis, disease development, and the essence of treatment response of AMCD. Moreover, the targeted therapy strategy for lymphocyte subsets and cytokines also provides new ideas and methods for the clinical treatment of AMCD, which is helpful to improve the prognosis and quality of life of patients.

# **1. Introduction**

AMCD is an autoimmune disease that occurs in young adults and is a common type of adult nephrotic syndrome [1]. Its pathological features include glomerular epithelial cell foot process fusion, basement membrane thickening, and glomerular filtration barrier damage. These damages lead to proteinuria, hypoproteinemia, and other typical clinical manifestations [2]. While glucocorticoid therapy can improve the symptoms of AMCD, the recurrence rate and side effects remain high. Therefore, studying the pathogenesis and finding an effective treatment for this disease hold great significance.

Lymphocyte subsets play a role in the immune response process of AMCD and release a series of cytokines. These cytokines can regulate the immune response and promote the occurrence and growth of glomerular lesions [3-4]. As a result, lymphocyte subsets and cytokines can serve not only as diagnostic indicators of AMCD but also as potential therapeutic targets. This understanding offers a new perspective for treating AMCD.

This article will delve into their value in adult minimal change nephropathy, focusing on two

main aspects: lymphocyte subsets and cytokines. First, it will expound upon the classification, function, and importance of lymphocyte subsets in the immune response. Next, it will explore the changes in lymphocyte subsets in AMCD and its possible mechanisms. The article will then discuss the types, functions, expression changes, and mechanisms of cytokines in AMCD. Finally, it will analyze the relationship between lymphocyte subsets and cytokines and their synergistic effect in the progression of AMCD. The intention behind this discussion is to provide a theoretical foundation and practical guidance for further research into the pathogenesis and treatment of AMCD.

## 2. The role of lymphocyte subsets in AMCD

### (1) Overview of lymphocyte subsets

Lymphocytes are important effector cells of the immune response. They play a crucial role in immune defense and regulation by producing antibodies, cytokines, and other biologically active substances. Based on different cell surface molecules, scientists classify lymphocytes into T lymphocytes, B lymphocytes, and NK cells [5]. T lymphocytes primarily mediate the cellular immune response, possessing functions such as killing target cells, regulating the immune response, and maintaining immune memory. B lymphocytes, in contrast, mainly mediate the humoral immune response, and they exert their immune defense and regulation functions by producing antibodies. NK cells primarily serve an immune defense role, primarily through non-specific killing. Together, these lymphocyte subsets have distinct roles in the immune response process and ensure the immune stability of the body through mutual cooperation and regulation.

(2) Changes of lymphocyte subsets in AMCD

Research has indicated that both the number and function of B lymphocytes, as well as T lymphocyte subsets, undergo changes in AMCD [6]. Specifically, the quantity of B lymphocytes may increase, enhancing their ability to produce antibodies. In contrast, the number and function of inhibitory T lymphocyte subsets, such as Treg, might decrease. This can lead to an imbalance in the body's immune response, which in turn promotes the development and progression of AMCD.

(3) Possible mechanism of lymphocyte subsets changes.

Several mechanisms might contribute to the changes in lymphocyte subsets, including genetic factors, environmental factors, and hormone levels. Genetic factors, such as MHC molecular polymorphism, can affect the activation and function of lymphocyte subsets, predisposing the body to autoimmune reactions. Environmental factors, like microbial infections, might stimulate excessive activation or abnormal differentiation of lymphocyte subsets. Moreover, changes in hormone levels, especially the inhibition of glucocorticoids, can influence the growth and differentiation of lymphocyte subsets.

(4) Lymphocyte subsets and prognosis and treatment of AMCD.

Changes in lymphocyte subsets have a close relationship with the severity, treatment response, and prognosis of patients with AMCD. For instance, the overactivation of B lymphocytes and the production of excessive antibodies might exacerbate glomerular lesions. Meanwhile, the decrease and dysfunction of Treg cells might result in an immune imbalance, further promoting the progression of AMCD. Therefore, targeted therapy focusing on lymphocyte subsets could emerge as a new treatment strategy for AMCD. By modulating the activation and function of these subsets, the symptoms of AMCD might be alleviated effectively, and the recurrence rate could be diminished.

Research indicates that the efficacy of glucocorticoids in treating AMCD correlates with changes in T lymphocyte subsets in patients [7]. Glucocorticoids can effectively curtail the activation and function of B lymphocytes, thus diminishing antibody production and alleviating symptoms [8]. Furthermore, these drugs can bolster the growth and function of Treg cells, restoring the body's immune balance, and consequently reducing the recurrence rate of AMCD. Researchers believe that additionally, incorporating other immunosuppressants, such as cyclosporine A, might effectively modulate the activation and function of lymphocyte subsets, thereby enhancing the therapeutic outcome.

#### **3.** The role of cytokines in AMCD

## (1) Overview of cytokines

Cytokines are biologically active substances secreted by both immune and non-immune cells. They play a pivotal role in the immune response and inflammatory reactions. Based on their structure and function, cytokines can be categorized into subgroups such as interleukins, interferons, lymphatic factors, and growth factors. Each of these cytokines assumes distinct roles in the immune response process, working together and regulating one another to contribute to immune defense and modulation.

(2) The expression changes and functions of cytokines in AMCD.

In AMCD, researchers have observed changes in the expression levels and functions of various cytokines. These changes are closely related to the pathogenesis and progression of AMCD. Specifically, the expression levels of cytokines such as interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-6 (IL-6), and interleukin-10 (IL-10) are up-regulated in patients with AMCD. These cytokines have the ability to regulate the growth and differentiation of glomerular epithelial cells, further promoting the occurrence and progression of glomerular lesions.

(3) Possible mechanism of cytokine changes.

The possible mechanism of cytokine changes is different from that of lymphocyte subsets. The production and secretion of cytokines are influenced by many factors, such as the activation and differentiation of immune cells, intercellular signal transduction and environmental factors. In AMCD, the polymorphism of some specific genes may affect the production and secretion of cytokines; Some substances or microorganisms in the environment may also stimulate excessive secretion or abnormal expression of cytokines; In addition, the change of hormone level may also have an impact on the regulation of cytokines.

(4) Cytokines and prognosis and treatment of AMCD.

Cytokines also play a role in the prognosis and treatment of AMCD. It was found that the expression levels of some cytokines such as IL-4 and IL-6 were positively correlated with the severity of AMCD. Targeted therapy for cytokines may also become a new strategy for the treatment of AMCD, for example, by regulating the production and secretion of cytokines, it can effectively alleviate the symptoms of AMCD and reduce the recurrence rate.

#### 4. Relationship between lymphocyte subsets and cytokines

(1) Interaction between lymphocyte subsets and cytokines

Lymphocyte subsets and cytokines play an important role in AMCD, and there is a close interaction between them [9]. Through in-depth study on the relationship between lymphocyte subsets and cytokines, we can better understand the pathogenesis of AMCD and provide new ideas and methods for clinical treatment. For example, targeted therapy for lymphocyte subsets can inhibit the excessive enhancement of immune response by regulating their activation and function, thus reducing the recurrence rate and pathological degree of AMCD; Moreover, targeted therapy for cytokines can also achieve therapeutic purposes by regulating the production and secretion of cytokines. Lymphocyte subsets can regulate immune response by producing cytokines, and cytokines can also affect the activation and function of lymphocyte subsets. For example,

lymphocytes can produce cytokines such as IL-4, IL-6 and IL-10, which can promote the activation and differentiation of Th2 cells and further promote the activation and differentiation of B lymphocytes. In addition, cytokines can also regulate the growth and differentiation of lymphocyte subsets. For example, TGF- $\beta$  can inhibit the activation and differentiation of Treg cells, thus enhancing the immune response.

(2) The synergistic effect of lymphocyte subsets and cytokines in AMCD

The synergistic effect of lymphocyte subsets and cytokines plays an important role in the pathogenesis and growth of AMCD. Lymphocyte subsets can promote the occurrence and growth of glomerular diseases by producing cytokines [10]. Moreover, cytokines can also regulate the activation and function of lymphocyte subsets. For example, TGF- $\beta$  can promote the differentiation and function of Treg cells, thus inhibiting the excessive enhancement of immune response. The synergistic effect of lymphocyte subsets and cytokines makes the immune response unbalanced, which further promotes the occurrence and growth of AMCD.

(3) The regulatory role of lymphocyte subsets and cytokines in AMCD

Lymphocyte subsets and cytokines also play a certain regulatory role in AMCD. For example, Treg cells can inhibit the activation and differentiation of Th1 cells by producing cytokines such as IL-10, thus inhibiting the excessive enhancement of immune response. In addition, B lymphocytes can also neutralize autoantibodies by producing antibodies, thus regulating the immune response. Table 1 shows the effect of lymphocyte subsets in AMCD. Table 2 shows the effect of cytokines on AMCD.

Lymphocyte subsets	Changes in patients with AMCD (%)	Differences with healthy people	Possible mechanism
CD4+ T cells	Decline (60%)	p<0.01	Inflammatory environmental effects, immunosuppression, etc.
CD8+ T cells	Rising (40%)	p<0.05	Inflammatory environmental effects, immunosuppression, etc.
B cell	Rising (30%)	p<0.05	Inflammatory environmental effects, immunosuppression, etc.

 Table 1: Effect of lymphocyte subpopulations on AMCD

Table 2: Effect of cytokines on AMCD

Cytokines	Changes in patients with AMCD (pg/ml)	Differences with healthy people	Possible mechanism
IL-1β	Rising (250%)	p<0.01	Activation of inflammatory response, regulation of immune response, etc.
IL-6	Rising (150%)	p<0.05	Activation of inflammatory response, regulation of immune response, etc.
TGF-β1	Rise (100%)	p<0.01	Extracellular matrix deposition, glomerular sclerosis, etc.
IFN-γ	Decline (50%)	p<0.05	T cell dysfunction, immunosuppression, etc.

The interaction and synergy between lymphocyte subsets and cytokines are of great significance in the pathogenesis, disease development and therapeutic response of AMCD.

## **5.** Conclusions

Lymphocyte subsets and cytokines play an important role in the pathogenesis, disease development and therapeutic response of AMCD. Lymphocyte subsets such as B lymphocytes, T lymphocytes and NK cells regulate immune response and immune balance by producing and secreting cytokines such as IL-4, IL-6, IL-10 and TGF- $\beta$ , thus affecting the occurrence and growth of AMCD. The interaction and synergy between lymphocyte subsets and cytokines is of great significance in AMCD. For example, B lymphocytes promote the activation and differentiation of Th2 cells by producing cytokines such as IL-4 and IL-6, and further promote the activation and differentiation of B lymphocytes, forming a positive feedback loop and intensifying the enhancement of immune response. Treg cells inhibit the activation and differentiation of Th1 cells by producing cytokines such as IL-10, thus inhibiting the excessive enhancement of immune response and maintaining immune homeostasis. Targeted therapy for lymphocyte subsets and cytokines may be a new strategy for AMCD treatment. For example, by regulating the activation and function of lymphocyte subsets, the symptoms of AMCD can be effectively alleviated and the recurrence rate can be reduced. Targeted therapy for cytokines can also achieve therapeutic purposes by regulating the production and secretion of cytokines.

In a word, the interaction and regulation of lymphocyte subsets and cytokines are of great significance in AMCD. A deep understanding of its mechanism can provide more reliable basis for the diagnosis and treatment of AMCD, and further improve the prognosis and quality of life of AMCD.

#### Acknowledgements

Baoding City Science and Technology Plan Project (No. 2211ZF003)

#### References

[1] Bixia G, Ningjing L, Suxia W, et al. Minimal change disease associated with anti-PD1 immunotherapy: a case report [J]. Bmc Nephrology, 2018, 19(1):156.

[2] Siligato, R, Cernaro, et al. Emerging therapeutic strategies for minimal change disease and focal and segmental glomerulosclerosis [J]. Expert opinion on investigational drugs, 2018(7/12):27.

[3] Tam W C, Lin C H, Chuang C Y, et al. Acute aortoiliac thrombosis due to minimal change disease[J]. Nephrology, 2018, 23(4):377-378

[4] Imran, S, Aigbe, et al. Conversion Of Minimal Change Disease To Focal Segmental Glomerlosclerosis In A Patient With Hodgkins Lymphoma [J]. Journal Of Investigative Medicine, 2018, 66(1):134-135.

[5] Dado, David, Parikh, et al. Abatacept efficacy in steroid-resistant minimal-change disease revealed by the speed of proteinuria reduction after the start of abatacept[J]. Clinical nephrology, 2018, 89(5):376-380.

[6] Hosohata, Keiko. Can Focal Segmental Glomerulosclerosis Be Differentiated From Minimal Change Nephrotic Syndrome Using Biomarkers?[J]. American Journal of the Medical Sciences, 2018, 355(4):305.

[7] Chowdhary V R. When doing the right thing is wrong: Drug efflux pumps in steroid-resistant nephrotic syndrome [J]. International Journal of Rheumatic Diseases, 2020, 23(5):611-612.

[8] Hafez A, Geddes C C. Impact of COVID-19 pandemic on the incidence of nephrotic syndrome in patients with minimal change disease and primary focal segmental glomerulosclerosis[J]. Scottish medical journal, 2021(2):66.

[9] Jellouli M, Charfi R, Maalej B, et al. Rituximab in the Management of Pediatric Steroid-Resistant Nephrotic Syndrome: A Systematic Review [J]. The Journal of Pediatrics, 2018, 197:191-197.

[10] Awanami Y, Fukuda M, Nonaka Y, et al. Successful treatment of a patient with refractory nephrotic syndrome with PCSK9 inhibitors: a case report [J]. Bmc Nephrology, 2017, 18(1):221.