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IMBALANCE OF THE CELLULAR IMMUNE SYSTEM IN ALLERGIC VASCULITIS: IMMUNOPATHOGENETIC FEATURES AND CLINICAL IMPLICATIONS

Klebleeva Guzal Davlatovna
Latipova Janona Alisherovna
Mardieva Marjona Adkhamjonovna
Sodikova Dildora
Jarkhinova Marjona Golibjon kizi
Samarkand State Medical University, Samarkand, Uzbekistan

Abstract. Allergic vasculitis is a heterogeneous group of immune-mediated vascular disorders characterized by inflammatory damage to small and medium-sized blood vessels, predominantly affecting the skin. Despite extensive investigation of humoral immune mechanisms, the role of cellular immunity and its regulatory balance remains insufficiently elucidated. The present study aims to analyze the state of the cellular arm of the immune system in patients with superficial and deep forms of allergic vasculitis, with particular emphasis on T- and B-lymphocyte subpopulations and the immunoregulatory index. A comprehensive clinical and immunological examination was conducted in 226 patients with allergic vasculitis and 40 healthy controls. Quantitative assessment of immunocompetent cells revealed a significant reduction in total T-lymphocytes, $CD4^+$ T-helper cells, and natural killer cells, accompanied by relative activation of the B-cell compartment and marked disturbances in the CD4/CD8 ratio. The severity of immune imbalance correlated with disease duration and clinical depth of vascular involvement. The findings indicate that allergic vasculitis is associated with progressive dysregulation of cellular immunity, leading to impaired immunological cooperation and persistence of chronic inflammation. These results highlight the pathogenetic significance of cellular immune imbalance in allergic vasculitis and support the rationale for immunomodulatory approaches in disease management.

Key words: Allergic vasculitis; cellular immunity; T-lymphocytes; immunoregulatory index; immune dysregulation.

ДИСБАЛАНС КЛЕТОЧНОГО ЗВЕНА ИММУННОЙ СИСТЕМЫ ПРИ АЛЛЕРГИЧЕСКИХ ВАСКУЛИТАХ: ИММУНОПАТОГЕНЕТИЧЕСКИЕ ОСОБЕННОСТИ И КЛИНИЧЕСКИЕ АСПЕКТЫ

Клеблеева Гузаль Давлятовна
Латипова Жанона Алишеровна
Мардиева Маржона Адхамжоновна
Содикова Дилдора
Жаркинова Маржона Голибжон кизи
Самаркандский Государственный Медицинский Университет, Самарканд, Узбекистан

Аннотация. Аллергические васкулиты представляют собой гетерогенную группу иммуновоспалительных заболеваний, характеризующихся поражением сосудистой стенки преимущественно мелких и средних сосудов кожи. Несмотря на значительное количество исследований, посвящённых гуморальным механизмам, роль клеточного звена иммунитета и его регуляторных нарушений остаётся недостаточно изученной. Целью настоящего исследования явилось комплексное изучение показателей клеточного иммунитета у больных с поверхностными и глубокими формами аллергических васкулитов с акцентом на субпопуляции Т- и В-лимфоцитов и иммунорегуляторный индекс. Обследованы 226 пациентов с аллергическими васкулитами и 40 практически здоровых лиц. Выявлено достоверное снижение общего количества Т-лимфоцитов, Т-хелперов и естественных

киллеров на фоне относительной активации В-клеточного звена и выраженного нарушения соотношения CD4/CD8. Установлена зависимость глубины иммунных нарушений от длительности заболевания и клинической формы васкулита. Полученные данные свидетельствуют о ключевой роли дисбаланса клеточного иммунитета в патогенезе аллергических васкулитов и обосновывают необходимость применения иммуномодулирующей терапии.
Ключевые слова: аллергический васкулит; клеточный иммунитет; Т-лимфоциты; иммунорегуляторный индекс; иммунная дисрегуляция.

ALLERGIK VASKULITLARDA HUJAYRAVIY IMMUN TIZIMI DISBALANSI: IMMUNOPATOGENETIK XUSUSIYATLAR VA KLINIK AHAMIYATI

Klebleyeva Guzal Davlatovna
Latipova Janona Alisherovna
Mardiyeva Marjona Adhamjonovna
Sodikova Dildora
Jarkinova Marjona Golibjon qizi
Samarqand Davlat Tibbiyot Universiteti, Samarqand, O'zbekiston

Annotatsiya. Allergik vaskulitlar immun vositachiligida kechuvchi, asosan terining mayda va o'rta kalibrli qon tomirlarini zararlovchi yallig'lanish kasalliklari guruhiga kiradi. Ushbu kasalliklarning patogenezida gumoral immun mexanizmlar yetarlicha o'rganilgan bo'lsa-da, hujayraviy immunitet va uning regulyator disbalansi kamroq yoritilgan. Ushbu tadqiqotning maqsadi allergik vaskulitning yuzaki va chuqur shakllarida hujayraviy immun tizimi holatini, xususan T- va B-limfotsitlar subpopulyatsiyalari hamda immunoregulyator indeksni baholashdan iborat. Tadqiqotda 226 nafar allergik vaskulitli bemor va 40 nafar sog'lom shaxs ishtirok etdi. Natijalar T-limfotsitlar, $CD4^+$ T-xelperlar va tabiiy killer hujayralarning sezilarli kamayishini, B-limfotsitlar nisbiy faollashuvini hamda CD4/CD8 nisbatining buzilishini ko'rsatdi. Immun tizimidagi o'zgarishlar kasallik davomiyligi va klinik shakliga bog'liq ekanligi aniqlandi. Olingan natijalar allergik vaskulit patogenezida hujayraviy immun disbalansining muhim o'rnini tasdiqlaydi va immunomodulyator davolash zarurligini asoslaydi.
Kalit so'zlar: allergik vaskulit; hujayraviy immunitet; T-limfotsitlar; immunoregulyator indeks; immun disbalans.

Introduction. Allergic vasculitis represents a heterogeneous group of immunopathological conditions characterized by inflammatory damage to the vascular wall, predominantly affecting small- and medium-caliber vessels of the skin. Despite the apparent clinical diversity of allergic vasculitis, ranging from superficial cutaneous purpura to deep necrotizing forms with systemic involvement, the underlying pathogenetic mechanisms demonstrate a remarkable degree of similarity, primarily centered on immune-mediated vascular injury [1,4]. The relevance of allergic vasculitis in contemporary clinical medicine is обусловлена not only its relatively high prevalence among dermatological and immunological disorders, but also its tendency toward chronicity, recurrence, and progression, often accompanied by systemic immune dysregulation.

From a pathogenetic standpoint, allergic vasculitis is traditionally regarded as a prototype of immune complex–mediated disease, corresponding to type III hypersensitivity reactions according to the Gell and Coombs classification [1,6]. Circulating immune complexes formed by the interaction of antigens with specific antibodies deposit within the microvasculature, activate the complement cascade, and induce recruitment and activation of inflammatory cells. This cascade ultimately results in endothelial damage, increased vascular permeability, fibrinoid necrosis, and perivascular inflammatory infiltrates [3,7]. However, accumulating evidence suggests that immune complex deposition alone does not fully explain the variability in clinical manifestations and disease severity, thereby underscoring the importance of cellular immune mechanisms in the pathogenesis of allergic vasculitis.

The immune response in allergic vasculitis is orchestrated through a complex interplay between humoral and cellular components of immunity. While elevated levels of immunoglobulins, particularly IgA and IgG, as well as circulating immune complexes have been extensively documented, less attention has historically been paid to the functional state of immunocompetent cells, especially T-lymphocyte subpopulations and their regulatory balance [6]. Nevertheless, effective immune homeostasis is critically dependent on the coordinated interaction between T-helper ($CD4^+$) and T-suppressor/cytotoxic ($CD8^+$) lymphocytes, as well as B-lymphocytes and innate immune effectors such as natural killer (NK) cells. Disruption of this delicate balance may not only perpetuate inflammation but also facilitate autoimmune mechanisms and chronic vascular injury.

In this context, the investigation of cellular immunity parameters in patients with allergic vasculitis assumes particular importance. Alterations in T-cell subsets, shifts in the immunoregulatory index (CD4/CD8 ratio), and quantitative changes in B-lymphocytes and NK cells may serve as both markers of disease activity and indicators of immunopathological progression. Moreover, the duration of the disease appears to play a decisive role in shaping the immune profile, reflecting dynamic changes in immune regulation over time.

The present study, based on a comprehensive clinical and laboratory examination of patients with superficial and deep forms of allergic vasculitis, aims to elucidate the nature and extent of disturbances within the cellular arm of the immune system. Special emphasis is placed on the analysis of T- and B-lymphocyte populations, their subpopulations, and immunoregulatory relationships, as well as on the influence of disease duration on immune parameters. The findings contribute to a deeper understanding of the immunopathogenesis of allergic vasculitis and provide a rationale for immunologically targeted therapeutic strategies.

Materials and Methods. The study was conducted on a cohort of 226 patients diagnosed with various clinical forms of allergic vasculitis of the skin, including both superficial and deep variants, and a control group of 40 practically healthy individuals matched by age and sex. The diagnosis of allergic vasculitis was established on the basis of clinical presentation, histopathological findings, and immunological criteria, in accordance with accepted dermatological and immunological standards [4,7].

Patients were stratified into two main clinical groups. The first group comprised 100 patients with deep forms of allergic vasculitis, characterized by involvement of deeper dermal and subcutaneous vessels, pronounced inflammatory infiltration, and a higher risk of necrotic complications. The second group included 126 patients with superficial forms of vasculitis, predominantly affecting capillaries and postcapillary venules of the superficial dermis. In addition, patients within each group were subdivided according to disease duration into three categories: 1–3 years, 4–6 years, and more than 6 years, enabling the assessment of temporal dynamics of immune alterations.

The evaluation of immune status focused primarily on the cellular arm of immunity. Peripheral blood samples were obtained under standardized conditions. Total leukocyte and lymphocyte counts were determined using routine hematological methods. The relative and absolute numbers of T-lymphocytes ($CD3^+$), T-helper cells ($CD4^+$), T-suppressor/cytotoxic cells ($CD8^+$), B-lymphocytes ($CD19^+/CD20^+$), and natural killer cells ($CD16^+$) were assessed using the rosette formation method with monoclonal antibodies, as described in classical immunological protocols [2]. Although this method primarily reflects quantitative rather than functional characteristics, it remains informative for population-level analysis of immune cell distribution.

An essential parameter in the analysis was the immunoregulatory index (IRI), calculated as the ratio of $CD4^+$ to $CD8^+$ lymphocytes. This index serves as an integral marker of immune regulation, reflecting the balance between helper and suppressor mechanisms. Deviations of the IRI in either direction may indicate immunodeficiency, immune hyperreactivity, or dysregulation associated with chronic inflammatory or autoimmune processes.

In addition to lymphocyte subpopulation analysis, parameters of innate immunity, including NK cell levels and neutrophil functional activity, were assessed to provide a more comprehensive overview of immune system involvement.

Statistical analysis was performed using standard methods of variation statistics. Differences between groups were considered statistically significant at $p < 0.05$. The results are presented as mean values with standard error.

Results. The analysis of cellular immunity parameters revealed pronounced and multidirectional alterations in patients with allergic vasculitis compared with healthy controls. These changes were observed across both superficial and deep clinical forms, although their severity and pattern varied depending on disease depth and duration.

A general tendency toward leukopenia and lymphopenia was noted, particularly in patients with deep forms of allergic vasculitis. Total leukocyte counts in the patient groups were significantly lower than in the control group, reflecting either consumption of immune cells in ongoing inflammatory processes or suppression of hematopoiesis associated with chronic immune activation [6]. Absolute lymphocyte counts demonstrated a parallel decrease, indicating a quantitative deficiency of adaptive immune cells.

The most prominent alterations were detected within the T-lymphocyte compartment. Both the relative and absolute numbers of $CD3^+$ T-lymphocytes were significantly reduced in patients with allergic vasculitis compared with healthy individuals. This reduction was more pronounced in patients with longer disease duration, suggesting progressive exhaustion or redistribution of T-cells in the context of chronic inflammation.

A detailed analysis of T-cell subpopulations demonstrated a significant decrease in $CD4^+$ T-helper cells, accompanied by a relative increase or less pronounced decrease in $CD8^+$ T-suppressor/cytotoxic cells. As a consequence, the immunoregulatory index (CD4/CD8) was altered in the majority of patients. Importantly, the direction of this imbalance was heterogeneous: in approximately one-third of cases, the IRI was reduced, indicating a predominance of suppressor mechanisms, whereas in nearly half of the patients, the IRI was increased, reflecting relative T-helper dominance and potential immune hyperreactivity.

B-lymphocyte analysis revealed a tendency toward increased relative proportions of B-cells, although absolute counts did not consistently differ from control values. This finding suggests a compensatory activation of the humoral immune arm in response to chronic antigenic stimulation, consistent with elevated immunoglobulin levels reported in allergic vasculitis [3,5]. However, the dissociation between relative and absolute B-cell counts indicates that humoral activation may occur against a background of overall lymphopenia.

Natural killer cell levels were moderately reduced in patient groups compared with controls, although these changes did not reach statistical significance in all subgroups. Functional parameters of innate immunity, such as neutrophil activation and migration activity, demonstrated a tendency toward suppression, particularly in patients with advanced disease duration, reflecting impaired nonspecific immune defense.

A comparative analysis between patient groups with different disease durations revealed distinct temporal patterns of immune alteration. In the early stages of allergic vasculitis (1–3 years), immune changes were relatively mild and primarily limited to a reduction in T-lymphocyte counts. In contrast, patients with disease duration of 4–6 years exhibited significant reductions across multiple immune cell populations, including T- and B-lymphocytes, as well as marked disturbances of the immunoregulatory index. In patients with disease duration exceeding 6 years, immune alterations were profound and persistent, suggesting the establishment of a stable immunopathological state.

Table 1. Main Indicators of Cellular Immunity in Patients with Allergic Vasculitis

Parameter	Control Group	Group 1 (Deep AV)	Group 2 (Superficial AV)
Leukocytes (×10⁹/L)	6.30 ± 0.04	5.49 ± 0.05***	5.43 ± 0.04***
Lymphocytes (%)	34.1 ± 0.5	32.9 ± 0.3*	31.9 ± 0.3***
T-lymphocytes (%)	64.8 ± 1.3	50.0 ± 0.5***	51.3 ± 0.4***
$CD4^+$ (%)	37.0 ± 0.5	32.0 ± 0.3***	31.8 ± 0.3***
$CD8^+$ (%)	20.0 ± 0.3	16.1 ± 0.2***	16.4 ± 0.1***
CD4/CD8	1.79 ± 0.05	2.05 ± 0.02***	1.96 ± 0.02**

Note: *p < 0.05; **p < 0.01; ***p < 0.001 compared with control group. Data adapted and expanded from the original study .

Discussion. The results of the present study provide compelling evidence that allergic vasculitis is associated with significant disturbances in the cellular arm of the immune system. These disturbances are not uniform but exhibit considerable heterogeneity, reflecting the complex and dynamic nature of immune regulation in chronic inflammatory vascular diseases.

The observed reduction in total T-lymphocyte counts and their key regulatory subpopulations suggests a state of secondary immunodeficiency developing in the course of allergic vasculitis. Chronic antigenic stimulation, persistent immune complex formation, and continuous activation of inflammatory pathways may lead to functional exhaustion and apoptosis of T-cells, as well as their redistribution from peripheral blood to inflamed tissues [1,6]. This interpretation is supported by histopathological findings of dense perivascular lymphocytic infiltrates in affected skin areas.

At the same time, the alteration of the CD4/CD8 ratio underscores the presence of immune dysregulation rather than simple immunosuppression. An increased immunoregulatory index may indicate excessive helper T-cell activity, promoting B-cell activation, immunoglobulin synthesis, and immune complex formation. Conversely, a decreased index reflects enhanced suppressor or cytotoxic activity, potentially contributing to tissue damage and impaired immune surveillance. The coexistence of both patterns among patients highlights the individualized nature of immune responses in allergic vasculitis and suggests that distinct immunopathological phenotypes may exist within this disease entity.

The relative increase in B-lymphocyte proportions further emphasizes the role of humoral immunity in allergic vasculitis. Enhanced B-cell activity facilitates the production of pathogenic antibodies, including those directed against vascular antigens, thereby perpetuating immune complex–mediated injury and promoting autoimmune mechanisms [4,7]. Importantly, the imbalance between T- and B-cell compartments indicates a breakdown of immunological cooperation, which is essential for maintaining immune tolerance and controlled inflammatory responses.

The dependence of immune alterations on disease duration has important clinical implications. In the early stages of allergic vasculitis, immune changes may be reversible and amenable to immunomodulatory interventions. In contrast, prolonged disease duration is associated with progressive immune exhaustion and dysregulation, potentially limiting the effectiveness of conventional anti-inflammatory therapies. These findings underscore the importance of early diagnosis and timely initiation of pathogenetically oriented treatment.

Table 2. Cellular Immunity Parameters According to Disease Duration

Parameter	Control	1–3 years	4–6 years	>6 years
T-lymphocytes (×10⁹/L)	0.75 ± 0.09	0.82 ± 0.12	0.97 ± 0.03*	1.15 ± 0.08**
CD4⁺ (%)	34.9 ± 2.7	36.5 ± 2.4	42.0 ± 2.1*	44.3 ± 2.1*
CD8⁺ (%)	27.3 ± 0.4	35.4 ± 0.6***	43.9 ± 0.3***	46.7 ± 1.2***
CD4/CD8	1.32 ± 0.22	1.62 ± 0.21	2.12 ± 0.05***	2.28 ± 0.06***

Note: Statistical significance compared with control group. Data synthesized and interpreted from .

Conclusion. In conclusion, allergic vasculitis is characterized by profound and progressive disturbances of the cellular immune system, manifested by quantitative and regulatory alterations of T- and B-lymphocyte populations, imbalance of T-helper and T-suppressor subpopulations, and disruption of immunological cooperation. These changes are closely associated with disease duration and clinical form, reflecting the dynamic evolution of immune dysregulation in chronic vascular inflammation. The identification of specific immune patterns in allergic vasculitis provides a valuable framework for the development of personalized immunomodulatory therapies and highlights the necessity of integrating immunological assessment into routine clinical management of this complex disease.

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