VIRAL DISEASES CAUSE NEGATIVE DISEASES TO THE HUMAN BODY

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Abstract. A literature review is devoted to the pathogenesis and clinical features of virus-associated glomerulonephritis in de tei. The types of viruses associated with glomerulonephritis are described. The mechanisms of kidney damage are analyzed, especially specificity of the course, therapy and prognosis depending on the type of virus. Attention is drawn to the fact that the combination immunosuppressive therapy with antiviral therapy improves treatment outcomes.

Keywords. Epstein-Barr virus, proteinuria, immunocomplex, virus-associated.

Protection of maternal and child health is a priority area of state social policy in Uzbekistan. The preservation and strengthening of the health of the younger generation is one of the priority directions among the state social tasks. One of the urgent problems of pediatric nephrology is the study of the frequency and nature of lesions of the urinary system in newborns.

The problem of glomerulonephritis attracts the attention of researchers in connection with the continuing increase in the incidence of this disease in children, a tendency towards a progressive course and an unfavorable prognosis due to the development of end-stage chronic renal failure - one of the common causes of early childhood disability [1].

Until now, glomerulonephritis remains the most important problem in pediatric nephrology. According to many researchers [8], chronic glomerulonephritis (CGN) is one of the main causes of chronic renal failure among acquired diseases in children. A number of researchers [7] believe that hypertension and proteinuria are the most important independent risk factors for the progression of kidney disease. Other factors responsible for the progression of renal dysfunction include dyslipidemia, anemia and impaired lipid metabolism [2] highlight the role of genetic risk factors in the progression of chronic kidney disease. At the same time, questions about the role of individual risk factors in the chronicity of glomerulonephritis in children remain unclear [1].

This opinion is shared by L.S. Prikhodina et al. [3]. Consider low birth weight as a risk factor for the progression of glomerulonephritis with a rapid decline in renal function and a high degree of resistance to immunosuppressive therapy [7].

The most frequent immunopathogenetic mechanism of development of glomerulonephritis is immunocomplex, which occurs in 70-80% of the total number of patients with glomerulonephritis [9].

Currently, all over the world, one of the urgent medical and social problems is herpesvirus infections. There are 8 known pathogenic antigenic serotypes of viruses belonging to this family: herpes simplex viruses type 1, type 2, chickenpox - herpes zoster, cytomegalovirus, Epstein-Barr virus, herpes viruses 6, 7 and 8 types. According to seroepidemiological studies, antibodies to HSV-1,2 are detected in 70-100% of the world's adult population, to EBV - in 95%, CMV - in 60%, HHV6 - in 80-100%.

A characteristic feature of all BBVIs is lifelong persistence in the body of an infected person, panthropism of organs and tissues, and the ability to cause multiple manifest forms of the disease, especially in conditions of the onset of immunodeficiency [5].

The role of BBVI in the development of a number of somatic diseases, including nephrological ones, has been proven [6]. Over the past decade, the role of streptococcal infection, as the main etiological factor of acute glomerulonephritis (AGN), has significantly decreased. The development and, especially, the progression of this pathology in children is increasingly associated with viral infections, including BBVI. Along with virus-induced immunopathological processes in patients with OHN, the role of persistence of viruses in the renal tissue is widely discussed in the literature [5].

Among the factors etiologically associated with the development of acute tubulointerstitial nephritis (ATIN), viral infections also occupy a special place. A direct and indirect cytotoxic effect of an infectious factor on various parts of the nephron with the development of disorders within renal hemodynamics was established. The pathogenesis of tubulointerstitial damage to the kidneys by viruses includes the effect on the renal tissue of the circulating virus in the blood, the development of immune complex damage with the deposition of immune deposits containing the pathogen antigen in the epithelium of the tubules or interstitium [12].

Kidney damage is one of the most common in cytomegalovirus infection. It was first described [5]. Cytomegalic metamorphosis predominantly undergoes the nephrothelium of the convoluted tubules, although sometimes glomeruli are involved in the process, replication of the virus in mesangiocytes is possible. Quite often, areas of lymphohistiocytic infiltration are detected in the kidneys [8].

However, the role of glomerulonephritis as an etiological factor is not clear. The question of what basic pathogenetic mechanisms determine the progression of glomerulonephritis in persistent and latent viral infection has been poorly studied. It should be noted that glomerulonephritis associated with a viral infection is characterized by a high frequency of exacerbations, mixed urinary syndrome in the form of proteinuria, hematuria, and resistance to immunosuppressive therapy [9].

The essence of the problem of cytomegalovirus infection is that the latter belongs to the so-called opportunistic infections, the clinical manifestation of which is possible only in conditions of primary or secondary immunodeficiency. The latent chronic

course characteristic of cytomegalovirus infection can turn into manifest forms. The provoking factors that weaken the body are therapy with glucocorticosteroids, cytostatics, intercurrent diseases, HIV infection, etc. [10].

According to studies, the determination of urinary excretion of MCP-1 can be used to monitor fibrogenesis in the interstitium of the kidney both in chronic glomerulonephritis [6] and in traumatic kidney damage [13]. Ischemic damage to the renal parenchyma is accompanied by the development of an inflammatory process with a possible outcome in nephrosclerosis. Monocyte chemoattractant protein-1 (Monocyte Chemoat tractant Protein-1, MCP-1) ensures the migration of mononuclear cells to the ischemia and inflammation zone, and is involved in the initiation and progression of tubulointerstitial damage [9].

Being a powerful chemokine and activator of cells of the mononuclear phagocyte system, MCP-1 potentiates the secretion of proinflammatory cytokines, promotes the migration of leukocytes into the infiltrate, and also ensures the proliferation of vascular smooth muscle elements [3]. An increase in the number of activated macrophages close to tubular epithelial cells leads to damage to the latter [12]. Activation of tubular cells by MCP-1 ensures their transdifferentiation into myofibroblasts [2], stimulating the synthesis of proinflammatory and prosclerotic components.

Undoubtedly, synthesis of viral homologues of the main immunosuppressive interleukin-10 (IL-10) plays an important role in virus-induced immunosuppression. Viral homologues are known for herpes viruses (Epstein-Barr virus, cytomegalovirus, herpes simplex virus) and smallpox viruses. The function of immunosuppression is determined by the ability of IL-10 to abolish the production of pro-inflammatory cytokines, while the main stimulating activity is directed to B-lymphocytes, for which IL-10 serves as a factor of survival and differentiation, as well as an increase in the production of immunoglobulins (Ig) A, M, G. The degree of homology of viral members of the IL-10 family, the human IL-10 molecule is 83%, and IL-10 of cytomegalovirus - only 27%. However, both homologues use the cell receptor IL-10 and mimic its main functions. It should be clarified that IL-10 of the Epstein-Barr virus reproduces only inhibitory, but not stimulating, effects of cellular IL-10 [9].

Viral homologues of cytokines and their receptors (have a profound effect on the physiology of the host immune system and can be considered as a suitable target for a new antiviral strategy. Many herpes viruses (Epstein-Barr virus, cytomegalovirus, herpes simplex virus) encode proteins that disrupt antigen recognition during inclusion of an antigen peptide into the binding site of the HLA class I. The products of cytomegalovirus genes block the assembly and transfer of this molecule to the surface of antigen-presenting cells, disrupt the IFN-γ-mediated expression of HLA class II molecules, and the herpes simplex virus suppresses the expression of HLA class II antigens on neurons.

The body's defense against viruses of the Herpesviridae family is provided by cellular immunity, primarily mononuclear cells, which are involved in a specific blastogenic response and antibody-dependent cytotoxicity, as well as natural killer cells. Humoral immunity does not provide protection against recurrence of herpesvirus infection [15].

Cytomegalovirus affects a variety of cells, most often all leukocytes (lymphocytes, monocytes), epithelial cells (respiratory tract, salivary glands, kidneys). From blood cells, cytomegalovirus with great constancy passes to the endothelium, the tropism to which it is extremely pronounced.Damaged endothelial cells are constantly found in the blood stream with active / reactivated cytomegalovirus infection; the presence of cytomegalovirus replication in them has also been proven. In addition, damage to the vascular endothelium has its own pathogenetic significance in the formation of organ lesions, as it causes ischemia or hemorrhages in various tissues. Cytomegalovirus is also characterized by the following features: the ability to replicate without damaging the cell; relatively low virulence; a sharp suppression of cellular immunity with a decrease in the immunoregulatory index of T4 / T8 lymphocytes, which can lead to generalization of the process. It is no coincidence that before the discovery of the human immunodeficiency virus, cytomegalovirus was assigned a leading role in the pathogenesis of acquired immunodeficiency syndrome.

The role of chemokines, such as IL-8, macrophage inflammatory protein-1α, monocytic chemotactic protein-1, soluble adhesion molecules VCAM-1 / ICAM-1, and L-selectin, in the formation of the latent course of cytomegalovirus infection has been established. Against the background of cytomegalovirus reactivation, with immunosuppression, a significant increase in the level of these chemokines was observed in patients with antigenemia [10].

The use of immunosuppressants and cytostatics after organ transplantation not only promotes the reactivation of previously acquired latent cytomegalovirus infection, but also increases the sensitivity of patients to primary infection with cytomegalovirus from seropositive donors. Antiviral therapy can increase the period of remission and affect the recurrence of infection, but does not allow the virus to be eliminated from the body [3].

The activity of endothelin-1 is determined by the polymorphism of the genotype, which is essential in the pathogenesis of hypertension, ischemic heart disease and is interrelated with the production of NO. The genetic basis of the regulation of the reningiotensin-aldosterone system with the participation of ACE and the contribution of rare polymorphisms to the increased risk of coronary heart disease, myocardial infarction, diabetic nephropathy are shown [5]. A high incidence of connective tissue dysplasia syndrome in children with various forms of glomerulonephritis has been established. The relationship between the clinical manifestations of glomerulonephritis

and the severity of connective tissue dysplasia was revealed: children with hormone-resistant nephrotic syndrome have more signs of connective tissue dysplasia (from 7 to 12) than children with a hormone-sensitive variant of nephrotic syndrome (5-7 signs). The levels of urinary excretion of cytokines and connective tissue metabolites differ depending on the variant of glomerulonephritis: increased urinary excretion of total oxyproline and its fractions is characteristic of chronic glomerulonephritis, an increase in the content of glycosaminoglycans in the urine is an indicator of an acute process in the kidneys in children. A significant increase in urinary excretion of monocytic chemoattractant protein-1 and inter-leukin-8 accompanies the development of renal tissue hardening processes. According to the results of the correlation analysis, a high degree of conjugation of indicators of urinary excretion of oxyproline and its fractions, glycosaminoglycans, monocytic chemoatractant protein-1 and interleukin-8 with laboratory indicators of manifestations of glomerulonephritis activity and its clinical course, the frequency of occurrence of signs of connective tissue dysplasia was revealed. An increase in the concentration of monocytic chemoattractant protein-1 and interleukin-8 in the urine is a criterion for a high degree of activity of the inflammatory process in the renal tissue, which is confirmed by laboratory parameters and the results of a morphological study of nephrobiopsy.

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