published: 30 December 2022
doi.org/10.56121/2181-2926-2022-8-05-10

Article

CLINICAL APPEARANCE AND TREATMENT TACTICS OF HERPESVIRUS ASSOCIATED NEPROPATHIES IN CHILDREN

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IJSP

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Received: 05 October 2022
Revised: 12 October 2022
Accepted: 12 November 2022
Published: 30 December 2022

Funding source for publication: Andijan state medical institute and I-EDU GROUP LLC.

Publisher's Note: IJSP stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Abstract: To date, among the etiological causes of chronic glomerulonephritis in children, the percentage of streptococcal infection has decreased, and at the same time, there are many records of nephropathies of viral etiology. 68 children were examined. Of these, 32 (47%) were children with chronic glomerulonephritis and 36 (53%) with nephrotic syndrome. All sick children underwent clinical, biochemical studies, as well as ELISA and PCR for the diagnosis of herpes infection.Conducted immunoserological studies in the group of children with chronic glomerulonephritis showed the detection of mono-CMV infection in 6.3%, HSV 1/2 +CMV infection in 6.3%, HSV 1/2 +CMV+HHV type 8 in 37.5% of children. In the group of patients with nephrotic syndrome, 10.1% had HSV 1/2 monoinfection, 8.3% had mono-CMV infection, 41.6% had HSV1/2+CMV, and 8.3% had HSV1/2+CMV+HHV 6 type, in 33.3% of HSV1/2+CMV+HHV type 8 mixed infection.

Keywords: chronic glomerulonephritis, nephrotic syndrome, herpesvirus infections.

Introduction. In recent years, there has been an increase in urinary tract diseases in children, and the share of microbial-viral kidney inflammation among them is 80%[6]. Failure to make an accurate diagnosis in time and late initiation of etiopathogenetic treatment leads to the exacerbation of the pathological process in the kidney, as a result, the development of chronic kidney failure. This memory, in turn, has a negative impact on the growth and development of the child, leading to disability [5]. To date, among the etiological causes of chronic glomerulonephritis and nephrotic syndrome in children, the percentage of streptococcal infection has decreased, and at the same time, there are many records of nephropathies of herpesvirus etiology [3]. It is known that herpesviruses (HV) belong to the group of airborne infections [1]. In the practice of pediatricians, herpesviruses are treated with the diagnosis of acute respiratory viral infection. In most cases, the acute respiratory viral infection lasts 3-5 days, and in some groups of children it lasts more than 10 days. This score predisposes children to various respiratory infections due to Epstein-Barr virus (EBV), cytomegalovirus (CMV), rhinovirus, adenovirus, RS-virus and types 1, 2, 6, 8 of herpes infection [4, 7].

In children, it is known that the immune system is formed during ontogeny, and Th-2 system immune process activity is observed from birth to 6 months. Later, the immune process is formed in the Th-1 direction in all age groups. The nasopharyngeal lymphoid system and epithelial tissue, which are intensively developing in early children, act as the first barrier to all acute respiratory viral infection. [5, 7]. A perfectly formed nasopharyngeal epithelial tissue is considered to be an organ that naturally has an adequate immune response to various viruses and bacteria. This mechanism is carried out with the help of anti-inflammatory cytokines, lysozyme, specific IgG. Inadequate activity of this immune barrier causes various viruses, including CMV, 1,2,4,6,8 type herpesviruses to damage

all organs through hematogenous and lymphogenous routes, including the formation of various nephropathies [8, 9].

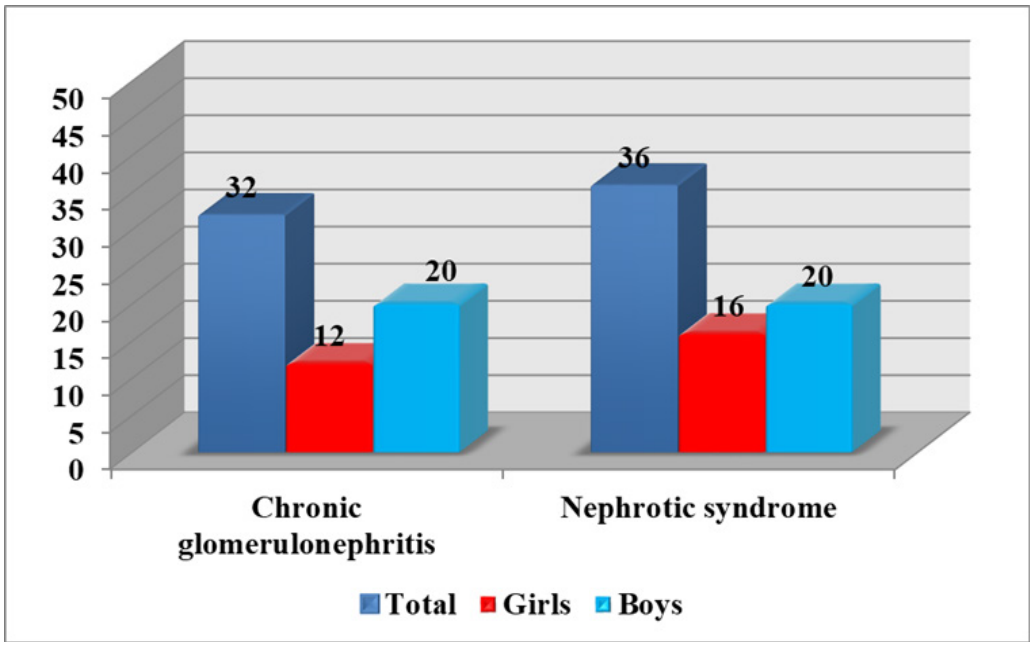
Herpesvirus infections (HVI) have the ability to persist in the body for a long time, in some cases for life. This creates a state of secondary immunodeficiency and serves as a basis for chronic diseases. In modern scientific literature, it has been determined that the level of cytotoxic activity of immune cells (T-killer, NK-cells) in damaged renal epithelial cells is related to the severity of the disease due to the direct cytopathic nature of HV [2, 10]. At the same time, the features of the clinical course and immuno-serological diagnosis criteria of viral association of chronic glomerulonephritis and nephrotic syndrome are not fully explained in practice.

The purpose of the study. Study of the clinical features of chronic glomerulonephritis and nephrotic syndrome with herpesvirus association in children and treatment.

Methods This study was conducted in 68 children of the Department of «Cardiorheumatology and Nephrology» of the multidisciplinary clinic of Tashkent Medical Academy. 32 (47%) of them had chronic glomerulonephritis (group I), 36 (53%) had nephrotic syndrome (group II) (Fig. 1). Chronic glomerulonephritis and nephrotic syndrome were diagnosed based on the 10th international classification of diseases. The age structure of the patients was 19 children in the age range of 12-16 years, 20 children in the age range of 7-12 years, 15 children in the age range of 3-7 years, and 14 children in the age range of 1-3 years. All patient children underwent ELISA and PCR to diagnose herpesvirus infection along with clinical analyses, biochemical tests. In the implementation of the ELISA method, using «Vector-Best» diagnostic kits, herpes simplex virus (HSV)1/2 IgM and IgG, cytomegalovirus (CMV) IgM and IgG, human herpes virus type 6 (HHV 6) IgG, human herpes virus type 8 (HHV 8) IgG was determined. The active type of herpes virus infection was established based on the data of specific IgM antibodies and viruria in urine. The latent type of herpesvirus was based on the recording of specific IgG antibodies only. Interpretation of the obtained results was carried out according to the

Figure 1.

General description of the examined children.



recommendations of the manufacturer of the diagnostic kit.

The results are processed using the Microsoft Excel program. We used Student's t-test to compare values between groups. A confidence difference of the corresponding statistical criterion $p<0.05$ was considered significant.

Results. Clinical studies showed that in 43.7% of group I, the disease was manifested in the nephrotic form of chronic glomerulonephritis, in 18.8% with symptoms of hematuria and proteinuria, and in 38% with symptoms of proteinuria and arterial hypertension. In 30.5% of patients of group II failure to respond to glucocorticosteroids, 69.5% had susceptibility to glucocorticosteroids (Table 1).

Table 1.

Level of manifestation of clinical symptoms in patients with chronic glomerulonephritis and nephrotic syndrome

Clinical signs	Level of encounter
Group I Chronic glomerulonephritis, n=32	
Nephrotic form	14 (43,7%)
Hematuria and proteinuria	6 (18,8%)
Proteinuria and arterial hypertension	12 (37,5%)
Group II Nephrotic syndrome, n=36	
Failure to respond to glucocorticosteroids	11 (30,5%)
Susceptibility to glucocorticosteroids	25 (69,5%)

When studying the life history and comorbidities of group I patients 37.5% had chronic tonsillitis, 18.7% had anemia, and 12.5% had enlarged adenoids. Clinical studies conducted in group II patients showed chronic tonsillitis in 42% of patients, anemia in 25%, adenoid gland enlargement in 17% (Table 2).

Table 1.

Level of manifestation of clinical symptoms in patients with chronic glomerulonephritis and nephrotic syndrome

Clinical signs	Level of encounter
Group I Chronic glomerulonephritis, n=32	
Chronic tonsillitis	12 (37,5%)
Anemia	6 (18,7%)
Enlargement of the adenoid gland	4 (12,5%)
No comorbidities were identified	10 (31,3%)
Group II Nephrotic syndrome, n=36	
Chronic tonsillitis	15 (41,6%)
Anemia	9 (25%)
Enlargement of the adenoid gland	6 (16,7%)
No comorbidities were identified	6 (16,7%)

The results of the epidemiological survey of mothers of sick children showed that 11% of patients had HVI markers previously detected, 13% of patients had no HVI markers, and 23% of patients were not previously

examined.

The results of our immunoserological study showed that in patients with chronic glomerulonephritis, CMV monoinfection occurred in 6.3% of patients, HSV 1/2 + CMV mixed infection in 50% of patients, HSV 1/2 + CMV + HHV type 6 mixed infection in 6.3% of patients, HSV 1/2+CMV+HHV type 8 was recorded in 37.5% of patients. 11.1% of patients with nephrotic syndrome have HSV 1/2 monoinfection, 8.3% have CMV monoinfection, 41.6% have HSV 1/2+CMV mixed infection, 8.3% have HSV 1/2+CMV+HHV type 6 mixed infection, HSV 1/2+CMV+HHV type 8 mixed infection was detected in 33.3% (Table 3).

Table 3.

Record of herpesvirus infection in patients with chronic glomerulonephritis and nephrotic syndrome.

Herpesvirus markers	Group I Chronic glomerulonephritis, n=32	Group II Nephrotic syndrome, n=36
HSV 1/2	0	4 (11,1%)
HSV 1/2 + CMV	16 (50%)	15 (41,6%)
CMV	2 (6,3%)	3 (8,3%)
HSV 1/2 + CMV+ HHV type 6	2 (6,3%)	3 (8,3%)
HSV 1/2 + CMV+ HHV type 6 and type 8	12 (37,5%)	12 (33,3%)

6 (18.7%) of children with chronic glomerulonephritis had an active type of herpesvirus, 11 (30.5%) of patients with nephrotic syndrome had an active type of herpesvirus.

Studies have shown that HV infection is more common in groups of children with chronic glomerulonephritis and nephrotic syndrome. At the same time, there was no correlation between indicators of severity of chronic glomerulonephritis, nephrotic syndrome and indicators of GV activity. This score indicates that herpesviruses act as a trigger in most scores. At the moment, recording of active herpesvirus infection in chronic glomerulonephritis and nephrotic syndrome groups indicates that it is appropriate to conduct long-term control and use of antiviral agents in these patients.

In a study group with chronic glomerulonephritis, antiviral treatment was conducted with valacyclovir for 10 days. In this case, the treatment doses were determined according to the age of the children. After 10 days, alpha-interferon-preserving suppositories (Viferon) were used 3 times a week for 3 months to strengthen the treatment results. The results of the study conducted in the main group of children showed that the main symptoms of the disease were weakness, the period of arterial pressure increase was convincingly reduced. At the same time, symptoms of rhinopharyngitis, lymphadenopathy, characteristic of herpesvirus infection, were significantly reduced compared to the control group. A positive periodic reduction was also observed in proteinuria, hematuria, and leukocyturia indicators recorded in urine analysis. This score was especially evident in the presentation of the hematuria scene. After 15 days, the DNA-HSV indicator was not recorded in 100% of patients with viral herpes association. This reflected that the treatment against the virus

had a positive result. At the same time, the indicators of tubular changes - leukocyturia and cylinduria - also showed a positive result.

Discussion. It is known that the properties of cellular and humoral immunity are determined by their number indicators, as well as their cytotoxic status, the ability to generate immunity against the virus through the production of interferon. Children with glomerulonephritis and nephrotic syndrome are at risk for secondary transient immunodeficiency. This is caused by immunosuppressant drugs used instead of pathogenetic treatment in most cases of glomerulonephritis and nephrotic syndrome. In a number of scientific studies [4, 8, 10], it has been proven that herpesviruses remain persistent infections in conditions of immunosuppression.

Herpesvirus-associated glomerulonephritis and nephrotic syndrome have specific treatment strategies. In these cases, first of all, the state of virus persistence and replicative activity indicate the appropriateness of antiviral treatment. In various scientific studies, drugs belonging to the atypical nucleoside group (valaciclovir, valganciclovir) have been shown to be effective in glomerulonephritis associated with herpesvirus 1/2, 4.5 types, and nephrotic syndrome. The main function of drugs of the atypical nucleoside group is to stop DNA polymerase activity in the viral genome [7]. Interferon α2 drugs (viferon) in glomerulonephritis of herpesvirus etiology, in addition to blocking the synthetic function of the viral protein, have the property of restoring cellular immunity, phagocytosis, and NK-cell activity [9].

Thus, herpesviruses play both an etiological and a trigger role in nephropathies observed in children, which in turn seriously affects the pathological process of the kidney. It is advisable to abandon cytostatic treatment during the active replication phase of herpesvirus. At the same time, it shows the need to take measures against the virus in a timely manner. It is not necessary to deny the association of HV infection in patients treated in nephrology departments of medical institutions, which shows that the development and implementation of special diagnosis and treatment algorithms is an urgent problem of today and there is a need for deep scientific research in this direction.

Conclusion.

1. In groups of chronic glomerulonephritis and nephrotic syndrome in children, herpesvirus infection manifests itself in the form of mono and mixed infection.

2. The relationship between the severity of chronic glomerulonephritis and nephrotic syndrome in children and the level of herpesvirus activity was not determined.

3. Record of herpesvirus infection in 18.7% and 30.5% of chronic glomerulonephritis and nephrotic syndrome in children shows that it is appropriate to use antiviral agents in these patients.

4. In children with active viremia of chronic glomerulonephritis herpesvirus association, it was found that the use of antiviral drug valaciclovir for 10 days is effective.

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