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Neurological manifestations of nervous system pathology in children with nephrotic syndrome

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Research Objective: Analysis of the main clinical-neurological manifestations of nervous system pathology in children with nephrotic syndrome (NS).
Patients and Methods: Thirty ostensibly healthy individuals and 100 children aged 7-15 with NS were examined. Chronic kidney disease (CKD) stages were determined according to the K/DOQI classification endorsed by the Congress of Pediatric Nephrologists of Russia. Patients were categorized into four groups based on CKD stages: 1st - CKD stage 1 (12); 2nd - CKD stage 2 (50); 3rd - CKD stage 3a (34); 4th - CKD stage 3b with signs of hepatic encephalopathy (24). Neurological status assessment was conducted in collaboration with neurologists, analyzing two main syndromes: asthenovegetative and encephalopathic. Digital data were processed using variational statistics.
Results: Asthenovegetative syndrome was more frequently observed in NS patients, particularly in children with CKD stage 3b and more prominently in the presence of hepatic encephalopathy. It manifested mainly as headaches and transient emotional lability. Additionally, clinical manifestations of encephalopathic syndrome were noted: anisoreflexia, paresis of cranial nerves VII – XII, coordination disorders, and horizontal nystagmus. The frequency of detecting anisoreflexia and horizontal nystagmus depended on the degree of impairment of kidney nitrogen excretory function, sharply increasing in the group of children with hepatic encephalopathy.
Conclusion: The obtained results emphasize the need for monitoring signs of hepatic encephalopathy and corresponding neuroprotection correction.
Keywords: children, chronic glomerulonephritis, renal encephalopathy, asthenic-vegetative syndrome, encephalopathy syndrome

Introduction: Due to the increasing frequency of nephrotic syndrome (NS) among all pediatric renal disorders and the necessity to prevent the development of chronic kidney failure (CKF), evaluating the course of NS has gained particular relevance [1,2]. The ultimate stage of NS progression is CKF, characterized by the clinical picture of uremia. Uremia disrupts the urea cycle, causes shifts in arginine metabolism, retains guanidine and its derivative - guanidinoacetic acid, accumulates toxic metabolites, and induces toxemia due to impaired excretion processes [3,4,5,6,7,8,9,10]. All these factors exert a toxic effect on various organs and systems [3], including the central nervous system (CNS), contributing to the development of renal encephalopathy (RE) [11,12,13,14,15,16,17].
The prevalence of nervous system involvement, the severity of its course, and often the lethal outcome of the disease make it crucial to study the clinical aspects, diagnostics, and issues of pathogenetic therapy.

Research Objective: To investigate the primary neurological manifestations of nervous system pathology in children with nephrotic syndrome (NS).
Patients and Methods: The study is based on the analysis of examination results of 120 children aged 7-15 years (mean age 11.83±0.27) treated at the TMA Medical Center and the city nephrological center from 2008 to 2011 for NS. Among them, 52 (43.3%) were aged 7-12 years, and 68 (56.6%) were aged 13-15 years. The average duration of NS was 4.32±0.78 years, ranging from 1 to 12 years. A control group comprised 30 conditionally healthy children of the same age.
All patients underwent a comprehensive examination, including biochemical and general clinical blood and urine tests, registration of hemodynamic parameters, and ultrasound examination of the kidneys. Considering that, in addition to the nosological form of the disease, the prognosis is influenced by the stage of chronic kidney disease (CKD), corresponding to a specific glomerular filtration rate (GFR), GFR values were determined using the Schwartz formula. CKD stages were determined according to the K/DOQI classification (2009) [3], approved by the VII Russian Congress of Pediatric Nephrologists (2011) [7,10]. The distribution

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of CKD stages revealed that the first three stages were the most common (Stage 1 – 12, Stage 2 – 50, Stage 3a – 34, and Stage 3b - 24). Notably, the last two stages (Stage 4 and Stage 5) were not identified in the examined patients.

Neurological status assessment was conducted in collaboration with neurologists. The presence of evident signs of hepatic encephalopathy (HE) was identified in 24 patients with CKD Stage 3b (significant decrease in GFR). Therefore, all patients were categorized into four groups based on CKD stages: 1st group – CKD Stage 1 (12 patients); 2nd group – CKD Stage 2 (50 patients); 3rd group - CKD Stage 3a (34 children); 4th group – CKD Stage 3b with evident signs of HE (24 patients). Digital data were processed using variational statistics with the Excel-70 computer program, employing the Student's t-test. Results were considered statistically significant at $P<0.05$.

Results: During the examination of patients, the diffuse nature of neurological disorders initially drew attention, manifesting through a variety of clinical symptoms. However, among the multitude of symptoms, we focused on two main syndromes: asthenovegetative and encephalopathic.

The asthenovegetative syndrome comprised subjective symptoms such as headaches, dizziness, sleep disturbances, and emotional lability. Objective symptoms included skin marbling, pronounced dermatographism, and increased sweating of the palms and soles. Among the 100 examined patients, manifestations of asthenovegetative syndrome, particularly headaches, were observed in 77 (64.2%) children, with the frequency increasing with the progression of CKD stages. The headaches were predominantly tension-type in 77.9% and hypertensive in 22.1%. Tension-type headaches occurred more often after the 2nd and 3rd lessons, localized in the occipitoparietal and frontotemporal regions. They intensified with stress and weather changes. Hypertensive headaches were accompanied by a feeling of pressure on the eye sockets, had a bursting character, occurred at night and in the mornings, primarily in patients with renal dysfunction in NS. Dizziness was observed in 28 (23.3%) patients with NS. It was predominantly nonsystemic and manifested as a sensation of "sinking," nausea, instability, and loss of balance. Systemic dizziness was characterized by a sense of object displacement during gaze fixation, body rotation, and swaying. Complaints of dizziness were more frequent in children of the 3rd and 4th groups. Sleep disturbances, manifested as difficulty falling asleep, occurred in 33 (27.5%) NS patients, especially those with moderate and significant GFR reduction. Emotional lability was present in 62 patients (51.7%), more prominently in children with impaired nitrogen excretory function and concomitant HE.

Encephalopathic syndrome was characterized by diverse focal neurological symptoms: heightened tendon and periosteal reflexes, anisoreflexia, coordination disorders, central paralysis of cranial nerves VII and XII. Neurological disorders were more common in patients with significant GFR reduction. Anisoreflexia occurred in 47 (39.2%) cases, mainly in those with renal function impairments. In the 3rd and 4th groups, this sign was identified in 52.9% and 70.8% of those examined, significantly higher than in children with preserved kidney function. Central paralysis of cranial nerves VII and XII was noted in 8.3% and 16.7% of children in the 1st group, 12% and 14% in the 2nd group, 26.5% and 29.4% in the 3rd group, and 37.5% and 41.7% in the 4th group. Another manifestation of encephalopathic syndrome was coordination disorders, predominantly observed in patients of the 3rd and 4th groups. Horizontal nystagmus was observed in 8.3% of patients in the 1st group, 28% in the 2nd group, 41.2% in the 3rd group, and 54.2% in the 4th group.

***Conclusion*:** Based on the obtained data, the following conclusions can be drawn:

1. Asthenovegetative syndrome was more frequently observed in NS patients, particularly in children with CKD Stage 3b, and more prominently in the presence of hepatic encephalopathy. It manifested mainly as headaches and transient emotional lability.
2. Children with NS exhibited clinical manifestations of encephalopathic syndrome, including anisoreflexia, paralysis of cranial nerves VII – XII, coordination disorders, and horizontal nystagmus. The frequency of detecting anisoreflexia and horizontal nystagmus depended on the degree of impairment of kidney nitrogen excretory function and sharply increased in the group of children with hepatic encephalopathy.

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