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КЛИНИКО-МОРФОЛОГИЧЕСКАЯ ХАРАКТЕРИСТИКА ПОЧЕЧНЫХ БИОПСИЙ ПЕДИАТРИЧЕСКИХ ПАЦИЕНТОВ С РАННИМ НАЧАЛОМ НЕФРОТИЧЕСКОГО СИНДРОМА

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CLINICAL AND MORPHOLOGICAL CHARACTERISTICS OF RENAL BIOPSIES IN CHILDREN WITH EARLY ONSET OF NEPHROTIC SYNDROME

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Резюме. В настоящее время отсутствует абсолютная гистологическая и клиническая схема для постановки диагноза генетически-детерминированного ФСГС, за исключением прямого назначения генетического тестирования. Анализ клинических данных и морфологических характеристик биопсий педиатрических пациентов с ранним нефротическим синдромом позволит найти возможные закономерности и обозначить пути для дальнейших поисков универсальной схемы диагностики генетически детерминированного ФСГС.

Ключевые слова: фокальный сегментарный гломерулосклероз, стероид резистентный нефротический синдром.

Resume. There are no absolute distinguishing patterns to differentiate genetic FSGS histologically or clinically from the other forms of FSGS except for a direct genetic testing. Clinical data analysis and morphological analysis of pediatric patients' renal biopsies with early onset nephrotic syndrome can assist in finding morphological and clinical correlations and identify possible ways in further search for the universal diagnostic scheme for genetically determined FSGS.

Keywords: focal segmental glomerulosclerosis, steroid-resistant nephrotic syndrome.

Relevance. Nephrotic syndrome (NS) is a clinical syndrome, characterized by massive proteinuria, low serum albumin levels, hyperlipidemia and edema. NS develops in patients with diverse kidney pathology. The early onset of NS is a possible marker of genetically determined focal segmental glomerulosclerosis (FSGS), as well as a positive family history, early age at onset of disease (~30% of FSGS with an onset before 25 years of age is genetic), and uncharacteristically severe and/or steroid-resistant disease [3]. Over 50 genes are currently known to be involved in FSGS, including, but not limited to podocyte-specific gene mutations in NPHS1, NPHS2, WT-1, LAMB2, CD2AP, TRPC6, ACTN4, PLCE1, SCARB2, ARHGDIA, DIAPH1, DIAPH3 and INF2 [3]. Genetic mutations are identified in sixty-one percent of the cases during the first year of life, in forty to sixty cases in young children, twenty-five to forty percent in older children, and only in ten to twenty five percent of the cases in adolescents [1].

Aim: the purpose of the research is to compare morphological and IHC changes in nephrotic syndrome (NS) with each other, and to identify their relationship with associated

morphological diagnoses and the frequency of their occurrence in pediatric patients within an early onset of NS.

Objectives:

1. Identify the correlations between the age, sex, onset age of the patients with the early onset of the NS and the pathological diagnosis.

2. Identify the correlations between the morphological changes and the pathological diagnosis;

3. Identify the correlations between the morphological features, such as glomerular, tubular, stromal sclerosis and the presence of Ig A, M, G, C3, C1q deposits.

Materials and methods. 55 results of pediatric renal biopsies of the patients with clinically diagnosed early onset nephrotic syndrome were analyzed. Histological slides were stained with hematoxylin and eosin, Schiff's reagent, Masson and MSB reagents. An IHC study was performed with antibodies to immunoglobulins (Ig) of classes A, M, G, and C3, C1q complement fractions. Statistical analysis of the information was performed using Microsoft Excel and Statistic 10.00.

Results and discussion. The first symptoms of NS (onset) have occurred between the ages of 1 and 3 years (yrs.) in 30 patients. Thirteen of the pediatric patients examined had their debut between 4 and 10 yrs. One child became ill at 12 yrs. Mean age of the disease onset is 2,1 yrs. (median – 2 yrs.). Male to female ratio (figure 1) is 33 (60%) to 22 (40 %).

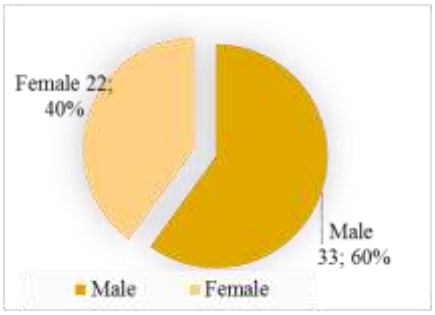

Fig. 1 – Percentage of males and females with the early onset of NS

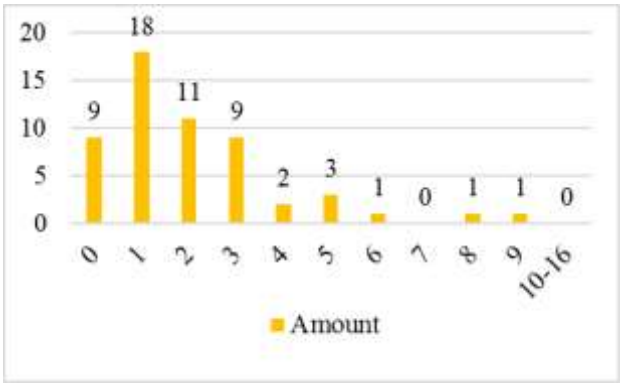

Fig. 2 – Onset age distribution

Morphological variants of renal lesions (figure 3) were represented by FSGS (47,3%, 26 children), minimal change disease (MCD) (21,8%, 12 patients), IgM-nephropathy (5,5%, 3 children) and mesangial proliferation without specific morphology (21,8%, 12 patients).

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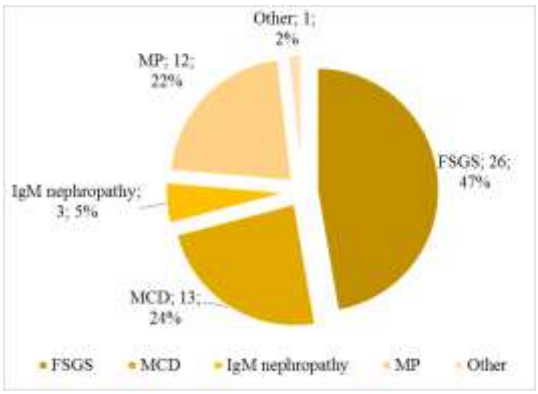

Fig. 3 – Morphological variants of NS

NS debuted acutely in 46 of 55 pediatric patients. In 9 of 55 cases, the first signs of the disease had included changes in the urinalysis in the form of proteinuria, or proteinuria combined with hematuria, and were detected during a routine check-up. 4 patients had NS with hematuria, 4 patients had NS with hypertension (HTN), and 8 patients experienced NS with hematuria and HTN at the moment of nephrobiopsy.

About fifteen percent of all NS is SRNS, which is characterized by proteinuria that does not cease within roughly six weeks of glucocorticoid treatment. Generally, about half of the patients with SRNS can experience remission with more intense immunosuppressive treatment, however the rest have multi-drug resistance and progress to chronic kidney disease and end stage kidney disease [2].

In our study the majority of the patients with an early onset of NS have as well developed SRNS. The mean age of the patients with SRNS is 5.1±4.5 yrs. (Me 3 yrs.), as well as the early onset of the renal symptoms was identified in the patients with developed SRNS with the mean age of 1.9±1.8 yrs. (Me 1 yr.).

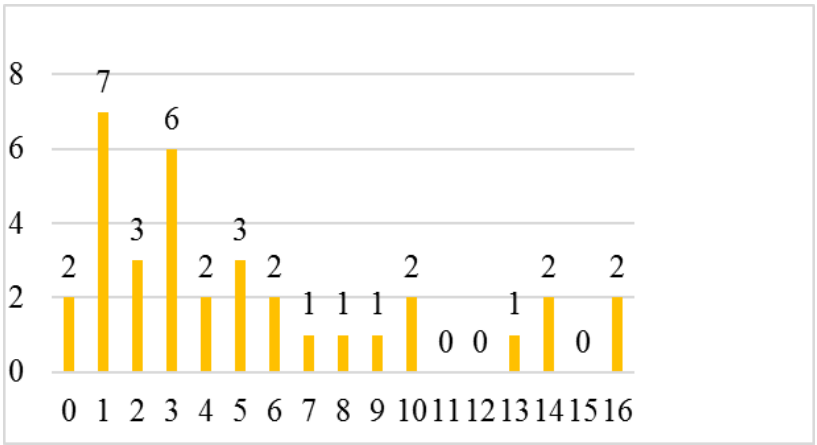

Fig. 4 – Onset age of SRNS

The majority of patients with steroid-resistant NS (SRNS) has FSGS (50,0%, 19 patients). Notably, there is a correlation between minimal change disease (MCD) and an unlikely presence of the SRNS (p=0,024). In the other cases, no statistical correlation between morphological diagnosis and the presence of SRNS has been established

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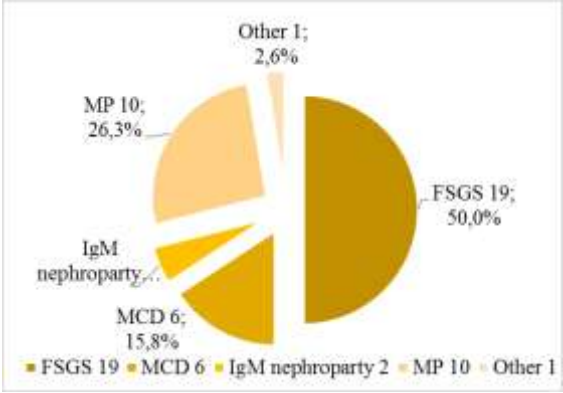

Fig. 5 – Percentage of SR morphological forms

According to the IHC data analysis of the sample data, there is a strong correlation between the global glomerular sclerosis and the glomerular deposition of IgM (p=0,04) and C3 (p=0,028) in the glomeruli (Fig. 6A), as well as a presence of the segmental glomerular sclerosis and the C3 (p=0,048) expression in the glomeruli (Fig. 6B).

The strong correlation is present between tubular sclerosis and the stromal depositions of IgA (p=0,025), IgG (p=0,001), IgM (p=0,048), as well as tubular deposition of C3(p=0,048) and C1q (p=0,007) deposition in the glomeruli. There is also a strong correlation between renal stromal sclerosis and the depositions of IgA (p=0,0001), IgG (p=0,004), IgM (p=0,004) in renal stroma.

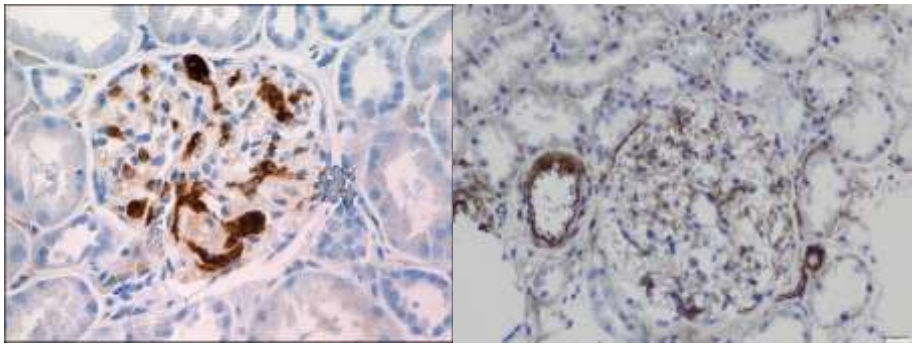

Fig. 6 – A: immunohistochemical expression of IgM in kidney glomerulus;
B: immunohistochemical expression of C3 in kidney glomerulus and artery wall.

Conclusions: in most cases early onset NS was accompanied by the development of the steroid resistant FSGS. More severe glomerulosclerosis is correlated with strong IgM and C3 expression in the glomeruli, whereas tubulointerstitial changes were more associated with IgM and IgA expression in the stroma and tubular expression of C3.

References

1. Differentiating Primary, Genetic, and Secondary FSGS in Adults: A Clinicopathologic Approach / An S. De Vriese, Sanjeev Sethi, Karl A. Nath and the others. // The Journal of the American Society of Nephrology. – . № 3. – С. 3-6.

2. Beata S Lipska-Ziętkiewicz. Genetic Steroid-Resistant Nephrotic Syndrome Overview / Beata S Lipska-Ziętkiewicz. // GeneReviews®. – 2021. – С. 2.

3. Importance of Genetic Diagnostics in Adult-Onset Focal Segmental Glomerulosclerosis / Rozemarijn Snoek, Tri Q. Nguyen, Bert van der Zwaag and the others. // Nephron. – . 2019. С. 352.