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CLINICAL AND LABORATORY FEATURES OF INTERSTITIAL NEPHRITIS IN CHILDREN WITH PURINE DYSMETABOLISM

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Abstract
The purpose of the study. Explore the clinical and laboratory features of the flow of interstitial nephritis in children that developed on the background of hyperuricemia and hyperuricosuria. Materials and methods. Examined 84 patients with an established diagnosis of interstitial nephritis dysmetabolic genesis background urikozurii more uric acid 1mg to 1ml of urine. Metabolic status of the patients was evaluated by a special program, which included a genealogical analysis, screening tests and quantitative biochemical studies. As the main biochemical marker to determine the level uricemia (> 320mkmol / l) and urikozurii. Results. Comparative analysis has shown that the difficulties can be overcome diagnosis by careful comparison of medical history, clinical and laboratory data and timely diagnosis urikozuric genesis nephropathy. Found that when dismetabolic interstitial nephritis unlike glomerulonephritis in the disease onset is no extra renal symptoms, does not suffer from glomerular filtration, azoth-excretory renal function. The diagnosis is confirmed by the presence of the characteristic spectrum of extra renal disease in the pedigree, the presence of hyperuricemia (> 0,310mmol / l) and urikozurii (> 1.0 mg uric acid 1ml urine). The most informative of the disease is the debut at an early age, the absence of extra renal symptoms in the presence of isolated bladder syndrome.

Keywords: children, hyperuricemia, hyperuricosuria, interstitial nephritis.

Introduction

Scientific progress and technological improvements have led to the emergence of such new areas of pediatric science and practice as metabolic pediatrics, environmental pediatrics. In recent years, it has been noted an increase in the frequency of renal pathology in childhood [2, 8]. A feature of the nosological structure of kidney diseases in recent decades is a significant increase in the frequency of dysmetabolic nephropathies [3], the proportion of which among diseases of the urinary system is, according to various authors, from 29 to 40% [11]. The features of the course and corrective therapy of pyelonephritis, which developed against the background of metabolic disorders, are being studied [6,12]. The most studied of the dysmetabolic nephropathies is the so-called dysmetabolic nephropathy with calcium oxalate crystalluria, which turned out to be a polygenically inherited multiple organ membranopathy with familial instability cytomembrane [1, 13]. Environmentally caused lesions of the tubulo-interstitial kidney tissue also manifest themselves in the form of dysmetabolic nephropathies [6], which is associated with the detection of mutant effect from a number of enzymes, in particular, those responsible for purine metabolism [7]. In recent years, dysmetabolic chronic interstitial nephritis has attracted the attention of researchers, among which urate nephropathies occupy a special place [6]. The frequency of urate

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nephropathies in the general pediatric population is 4.2%, and among the registered renal pathology - 9.9% [13]. Age-related features of the manifestation and course of urate nephropathies It is under study [16,19,21]. Due to the intensity of purine metabolism in a growing body, pathological syndromes caused by hyperproduction of uric acid (MC) in children are more common than diagnosed.

The purpose of this work is to study clinical and laboratory features of the course interstitial nephritis developed in children against the background of hyperuricemia with hyperuricosuria.

Materials and Methods

84 patients with interstitial nephritis on the background of uraturia aged from 1 to 17 years were under observation. The metabolic status of patients was assessed based on the results of multiple studies conducted according to a multi-stage special program that included genealogical analysis, screening tests and quantitative biochemical studies. The main biochemical marker of impaired purine metabolism was the level of uricemia and uricosuria according to Muller-Seifer, daily urinary excretion of urates by Hopkins method [10], oxalates according to N.V. Dmitrieva [3]. Due to the lack of studies highlighting the functional state of the kidneys in children with nephropathies of metabolic origin in the climatic conditions of Uzbekistan, we used a set of indicators that quantitatively characterize partial kidney functions: glomerular function was assessed by Van Slyke endogenous creatinine clearance, tubular functions by Zimnitsky's test, urine osmolarity by cryoscopic method on the OMK-I apparatus C0I, ammonia and titrated acids in the description of I. Todorov [12]. In addition to special studies, data from general clinical studies and X-ray planimetry of excretory urograms were taken into account. Hyperuricemia was considered to have a serum uric acid level of more than 320 micromol/l, hyperuricosuria -with urinary excretion of more than
1 mg per 1 ml of urine [13].

Research Results and Discussion

A comparative retrospective analysis of the conditions of manifestation of interstitial nephritis (IN) against the background of uraturia shows that the complexity of the clinical diagnosis of the disease is explained by their insufficient knowledge at the early stages of the disease development. Of the 84 children, 39 were referred with a diagnosis of acute and chronic glomerulonephritis (46.4%), 23 acute pyelonephritis (27.4%) and 22 recurrent urinary tract infection (26.2%), 82% of patients from 1 month to 2 years received conventional treatment according to the established diagnosis without sustained effect. Long-term, sometimes persistent treatment in these cases is associated with an unjustified risk of various side effects, in the absence of positive results. Meanwhile, a comparative analysis shows that with the correct interpretation of clinical and generally accepted laboratory data, timely diagnosis of kidney lesions of metabolic origin is possible. Thus, interstitial nephritis on the background of uraturia is characterized by early manifestation in the form of an isolated urinary syndrome (Table.1), the absence of extrarenal signs in the early stages (edema, hypertension). Urinary syndrome was detected for the first time in 42 children under the age of 3 years (51.2%), in 27 (32.9%) 4-7 years and in 13 children after 8 years (15.8%) against the background of acute respiratory viral infections, pneumonia and gastrointestinal diseases in 62 cases (75.6%), and the rest they were revealed accidentally during an examination for another reason. Enuresis was observed in 8 children (9.8%), abdominal syndrome in 21 (25.6%).

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Table 1 **Clinical and laboratory comparative data**

Indicators	Groups		
	Healthy (n=27)	Patients with Glomerulonephritis (22)	Patients with Interstitial (n=84)
Urinary syndrome detected against the background of infectious diseases	-	7 (31,8%)	66 (78,6%)
The presence of an interval of at least one week after the disease	-	12 (54,5%)	14 (16,6%)
Accidental detection	-	-	21 (25 %)
Swelling	-	22 (100%)	29 (34,5%)
Hypertension	-	18 (81,8%)	9 (10,7%)
Residual nitrogen (mmol/l)	0,2±0,02	22 (100%)	33 (39,2%)
Cholesterol (mmol/l)	15,7±1,4	30,3±2,1 P<0,005	29,4±1,4 P>0,05
Total protein (g/l)	4,84±0,4	8,8±0,91 P<0,005	7,43±0,85 P<0,005
Creatinine clearance (ml/min 1.73 m2)	72,0±2,5	61,0±1,5 P<0,05	67,7±3,0 P>0,05

Children did not lag behind their peers in physical development, the well-being of sick children remained satisfactory, and the children were active. Hematuria prevailed over leukocyturia in all children, and transient macrohematuria was noted in 12 children. Moderate pasty of the face, mainly in the morning, occurred in 18 children (20.5%). A "family portrait" of the extrarenal pathology of children with uraturia is characteristic: a high incidence among adults (parents and other relatives) of diseases such as urolithiasis and cholelithiasis, gout, hypertension, obesity, diabetes mellitus among siblings, neuroarthritic diathesis, biliary pathology. Thus, in dysmetabolic interstitial nephritis, unlike GN, glomerular filtration, nitrogen excretion function of the kidneys, and nonspecific indicators of the inflammatory process do not suffer at the onset of the disease, which is undoubtedly diagnostic value. Data on partial renal functions in patients with IN on the background of uraturia are of interest (Table 2).

As can be seen from Table 2, in patients with urate nephropathy without signs of activity of the nephritic process, the filtration and osmoregulatory function of the kidneys were not changed (P>0.5). At the same time, there was a significant decrease in urinary excretion of ammonia (33.6±1.76 mmol/day, P<0.001) and an increase in the level of titrated acids (0.74±0.08 mmol/day, P<0.05). In patients with urate nephropathy, there was a simultaneous increase in the level of oxaluria (0.66±0.05 mmol/ day., at a rate of 0.38±0.06 mmol/day, P<0.05) the ratio of oxalates to excreted creatinine (P<0.001), the level of phosphaturia and calciuria (P<0.05). Exacerbation of interstitial nephritis and layering of pyelonephritis leads to a significant aggravation of disorders of partial renal functions. Thus, in this group there was a significant (respectively 92.0±10.4 and 60.4±5.6 ml/min 1.73 m2) decrease in renal filtration function (P<0.005), urine osmolarity (P<0.05) and ammoniogenetic renal function (respectively 33.6±1.76 and 24.7±1.76 mmol/day, P<0.05). The level of titrated acids increases slightly, significantly exceeds the level of uricosuria, oxalate, calcium, phosphaturia (P<0.05). The ratio of urates to creatinine is 1.92±0.38 with a norm of 0.85±0.08, (P<0.05).

Table 2. Partial renal function in patients with urate nephropathy depending on the activity of the renal process (M±m)*

Indicators	Groups		
	Healthy (n=27)	Uraturia without nephropathy (n=20)	Interstitial nephritis on the background of uraturia (n=21)
Diuresis (ml/day)	1080±17,0	680,0±14,0 P<0,005	907,0±20,0 P<0,005
Creatinine clearance ((ml/min 1.73 m2)	115,8±7,1	97,3±4,7 P<0,005	107,±19,8 P<0,005
Ammonia (mmol/day)	53,3±1,18	33,2±1,76 P<0,001	23,9±1,77 P<0,001
Titrated acids (mmol/day)	0,43±0,07	0,75±0,08 P	0,97±0,15 P<0,005
Urates (mmol/day)	2,94±0,27	6,17±0,56 P	6,37±0,47 P<0,005
Urates/ Creatinine	0,85±0,08	1,7±0,14 P<0,05	1,98±0,35 P<0,001
Oxalates (mmol/day)	0,38±0,06	0,66±0,05 P	0,94±0,08 P<0,001
Oxalates/ Creatinine	0,053±0,005	0,17±0,02 P<0,001	0,21±0,03 P<0,001
Calcium (mmol/day)	51,5±2,75	62,5±4,0 P<0,05	75,0±87 P<0,005

*-note: P is the reliability of the difference compared to healthy people.

Consequently, in patients with urate nephropathy, unlike patients with glomerulonephritis , a violation of the homeostatic functions of the renal tubules, osmoregulatory and ammonioacidogenetic functions is observed already at the early stages of development. Thus, despite the paucity of clinical manifestations of interstitial nephritis, a thorough assessment of family history, features of partial renal function allows early diagnosis and differentiated therapy.

Conclusions

Dysmetabolic interstitial nephritis is characterized by manifestation at an early age, absence of extrarenal symptoms at the onset in the presence of isolated urinary syndrome. Interstitial nephritis against the background
of uraturia is characterized by an early violation of the homeostatic functions of the tubular kidney system. The most informative for the diagnosis of dysmetabolicnterstitial nephritis are the state of osmoregulatory and ammonioacidogenetic renal function.

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