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The Course of Juvenile Idiopathic Arthritis and Kidney Damage

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Abstract The study of the course of juvenile idiopathic artritis (JIA), determination of disease activity, duration, number of affected joints and target organs improved the understanding of the pathogenesis of the disease and made it possible to better characterize the reliability of use in therapy. The aim of the study was to research various variants of the course of JIA and kidney damage. Tested 38 patients aged 3 to 17 years with JIA and a questionnaire, clinical, anamnestic and laboratory-instrumental examination were conducted. Results of the study showed that 29-76.3% patients characterized criteria as arthritis lasting 3 months or more, morning stiffness, arthritis of the second joint that arose after 3 months and later, symmetrical damage to small joints, effusion into the joint cavity. In 28.9% patients, a persistent variant of oligoarthritis was noted, and progressive oligoarthritis occurred in 71% of the examined patients. In 60.5% patients, the disease proceeded with kidney damage. The duration of the course in JIA in children ranges from 3 months to 8 years, large and medium joints are more often affected - knee, ankle, wrist, elbow, hip. The exudative component of 39% is less pronounced in boys, productive-dystrophic changes of 61% in the joints of the lower extremities predominate. In girls, exudation in the joints of the upper extremities prevailed - 85%. Kidney damage in the form of nephritis was observed in 60.5%, microalbuminuria - in 13.2%, an increase of creatinine data in the blood – 68%.

Keywords Juvenile idiopathic arthritis, Children, Damage, Kidney, Glomerulonephritis, Acute or chronic interstitial nephritis

1. Introduction

Juvenile idiopathic arthritis (JIA) is a destructive and inflammatory joint disease with unknown etiology, complex immunoaggressive pathogenesis, which is characterized by symmetrical chronic arthritis, systemic damage to internal organs, leading to disability in sick children [1]. In this regard, the problem of improving the efficiency of correction optimization in JIA remains extremely relevant, both from the point of view of scientific and practical pediatrics. The leading risk factors for reduced life expectancy in JIA are diseases of the cardiovascular system, damage to the urinary tract, gastrointestinal tract, infections, and lymphoma [3]. Kidney pathology occurs in JIA with a high frequency - from 57 to 73% according to different authors [8]. With this disease, urinary tract infections, cystitis, pyelonephritis, glomerulonephritis, secondary amyloidosis of the kidneys, acute or chronic interstitial nephritis, chronic kidney disease, papillary necrosis, vasculitis of the renal vessels can be observed. In most patients with JIA, kidney damage determines the prognosis and outcome of the disease [4]. Idiopathic arthritis is a systemic disease that can affect internal organs. In most cases, this is due to the kidneys. Kidney damage in idiopathic arthritis is the most common cause of death from this disease [6].

There are kidney lesions that are directly related to the disease itself, and iatrogenic lesions that are associated with the effects of drug therapy. And often, treatment for juvenile idiopathic arthritis hastens or precipitates kidney damage. Glucocorticoids and cytostatics reduce renal function, which leads to their diseases [5].

Most drugs used to treat JIA can cause kidney damage. This is due to their direct nephrotoxic effect or through the body's immune response mechanisms [7]. To assess the severity of renal damage in autoimmune diseases, it is recommended to use the index of chronicity as an additional indicator. If the chronicity index is high, kidney changes are irreversible, immunosuppressive therapy is ineffective, and this, in turn, is considered a poor prognostic sign. Changes in the kidneys are usually diffuse in nature with an outcome in chronic renal failure and renal amyloidosis [11]. All this dictates the need to optimize early diagnosis, prognosis, correction and prevention of complications from the urinary

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system in juvenile idiopathic arthritis. Kidney damage in JIA occupies a special place among other systemic manifestations of this disease and has a huge impact on the prognosis of the disease, approaches to its therapy, and outcome [9]. According to various authors, renal pathology occurs in 20-75% of patients with this disease [10]. In terms of the frequency of kidney damage, JIA ranks third among rheumatic diseases, second only to such diseases as SLE and SV.

The structure of rheumatoid nephropathy is diverse and includes changes that are either pathogenetically associated with the disease itself (secondary amyloidosis, glomerulonephritis, tubulointerstitial nephritis (TIN)), or as an extra-articular manifestation (renal vasculitis), or associated with drug therapy.

Renal changes are characterized by the early onset of non-sustained leukocyturia and mild proteinuria and hematuria, and are most often observed at the onset of the disease or during its exacerbation, and are also associated with the activity and severity of JIA [2].

The aim of this study was to study various variants of the course of JIA and kidney damage.

2. Materials and Methods of Research

To determine the nature of kidney damage in patients with juvenile idiopathic arthritis, 38 children with JIA were examined and a questionnaire, clinical, anamnestic and laboratory-instrumental examination were conducted. The studies were carried out on the basis of the cardio-rheumatology department of the Tashkent medical academy multidisciplinary clinic. Of the 38 patients, there were 20 (52.7%) girls and 18 (47.3%) boys aged 3 to 17 years (mean age 10 years). The duration of the disease ranged from 3 months to 8 years. Girls predominated among the examined patients depending on gender.

The great number of patients (more than 50%) were children with a disease period of up to 1 year, more than 5 years of disease was in 2 observed children. The timing of diagnosis ranged from 4 months to 3 years. The diagnosis was established in accordance with the classification of juvenile idiopathic arthritis according to the second version of ILAR "International League of Associations for Rheumatology" and ICD-10.

Despite the sufficient clarity of the criteria for early diagnosis of JIA, more than a year to diagnose the disease in the patients we observed in more than a third of cases, and only 13 (34.2%) patients were diagnosed intime. Considering the aggressiveness of the course of JIA, the timing of the diagnosis is important, because timely treatment leads to a further favorable prognosis of the disease.

3. Research Results and Discussion

We analyzed the frequency of occurrence of diagnostic clinical criteria for JIA among the examined groups of patients. The absolute majority of the examined patients (29-76.3%) were characterized by such criteria as arthritis lasting 3 months or more, morning stiffness, arthritis of the second joint that arose after 3 months and later, symmetrical damage to small joints, effusion into the joint cavity. In the affected joint, pain, swelling, deformity and limitation of movement, an increase in local skin temperature were noted. Large and medium joints were more often affected - in 26 (68.4%) knee, ankle, wrist, elbow, hip joints. In 7 (18.4%) patients there was a lesion of the cervical spine, in 5 (13%) patients bilateral sacroiliitis, in 1 (2.6%) the disease was accompanied by Raynaud's syndrome and in 1 (2.6%) the patient was accompanied by a genetic disease mucopolysaccharidosis, Hunter type (table 1).

Table 1. Clinical forms and course of JIA

№	Indicators	Number of patients	%
1	Arthritis lasting 3 months or more	29	76,3
2	Damage of large and medium joints	26	68,4
3	Damage of the cervical spine	7	18,4
4	Bilateral sacroiliitis	5	13
5	Raynaud's syndrome	1	2,6
6	Mucopolysaccharidosis	1	2,6
7	Persistent variant of oligoarthritis	11	28,9
8	Progressive oligoarthritis	27	71
9	Exudative component	7	39
10	Productive-dystrophic changes	11	61
11	Articular-visceral form	10	26,3%
12	Kidney damage	28	60,5
13	Heart damage	2	5,2
14	Lung damage	1	2,6
15	Combined lesions of internal organs.	4	10,5

In 11 (28.9%) patients, a persistent variant of oligoarthritis was noted, characterized by the fact that up to 4 joints were affected during the entire period of the disease. Progressive oligoarthritis occurred in 27 (71%) of the examined patients and was characterized by an increase in the number of affected joints after 6 months of illness.

Some features of the articular syndrome have been established depending on the form of the disease, the nature of the course of JIA, the sex and age of patients. Thus, the articular form of the disease with a subacute onset was accompanied by the development of arthritis with a predominant lesion of the knee and ankle joints (68% and 28%, respectively). In the future, the wrist and elbow joints joined more often than others. At the same time, the process progressed moderately and productive changes prevailed. X-ray was determined mainly II degree according to Steinbrokker. In the acute onset of this variant of the disease, the wrist, metacarpophalangeal and interphalangeal joints of the hand were more often involved in the process.

The study of the characteristics of the articular syndrome

depending on gender showed that the exudative component is less pronounced in boys (7-39%), productive-dystrophic changes (11-61%) in the joints of the lower extremities (hip, knee, ankle, foot joints) predominate, the idiopathic factor in blood serum is determined extremely rarely. In girls at the initial stages of the disease, exudation prevailed in the joints of the upper extremities - the wrist, elbow, small joints of the hand (17-85%).

The articular-visceral form was noted in 10 (26.3%) of the patients and clinically characterized by a high temperature reaction, which was of an intermittent nature and did not decrease during antibiotic treatment.

In 28 (60.5%) patients, the disease proceeded with kidney damage, in 5.2% of patients with heart damage, in 2.6% - with lung damage, in 10.5% - there were combined lesions of internal organs. In systemic forms, the articular syndrome also had its own distinctive features. So, in one patient with an allergic-septic variant, the disease began with persistent arthralgia in large (knee, hip) and medium (ankle, wrist and elbow) joints without visible changes in them.

The first degree of disease activity was established in 11 (28.9%) patients with lesions of no more than 4 joints, with minimal ESR values up to 20 mm/hour, with a normal level of C-reactive protein (CRP); the second degree was documented in 19 (50.1%) patients with intermittent arthritis and ESR values of not more than 40 mm/hour, borderline elevated CRP; the third degree was registered in 8 (21%) children, in the presence of systemic manifestations of arthritis, a large number of swollen and painful joints, duration of morning stiffness for more than an hour and high humoral activity - high CRP and / or positive RF, ESR > 40 mm / h. In half of the examined patients, the first stage of anatomical changes according to Steinbrokker was noted, i.e. - epiphyseal osteoporosis, in 1/3 of the patients we noted narrowing of the joint space and the presence of single erosions. Cartilage and bone destruction occurred in three patients (7.8%) with a disease period of more than 3 years.

Among the examined children with JIA were identified kidney damage in the form of nephritis (Table 2).

Table 2. Kidney damage in JIA

№	Indicators	Number of patients	%
1	Urinary syndrome	28	60,5
2	microalbuminuria	7	13,2
3	Increasing the concentration of albumin in the urine more than 20 mg/l	12	42,8
4	Increase in blood creatinine	19	68

An analysis of the frequency of nephritis in patients with JIA was carried out, and it was found that the urinary syndrome was detected in 28 (60.5%). When distributing by gender, girls predominated in all groups. The age of children with JIA with kidney damage during the observation period was on average the same and amounted to 7 years. Moreover, children with JIA at the beginning of the observation with kidney damage were significantly older than in the group without nephritis ($p < 0.05$). Therefore, the duration of JIA disease in the group of children with nephritis was significantly higher than in patients without kidney damage ($p<0.05$).

Laboratory studies have shown that significantly more often in children with secondary nephritis in JIA compared with children who did not have kidney damage, anemia was detected (grade 3 in 4 - 10.8% of children with kidney damage and 1 - 1.2% without lesions), accelerated ESR (40 mm / h in 15 - 40.5% of patients with kidney damage and in 6 - 7.1% without nephritis). There was also an increase in the level of leukocytes, stab and segmented neutrophils, but without significant differences.

The functional state of the kidneys in patients was assessed in accordance with the content of creatinine. Thus, among the examined sick children with JIA, the content of creatinine in the blood in children with kidney damage was significantly higher 19 (68%) out of 28 than in children without kidney damage 6 (15%).

An early sign of kidney damage in various diseases is microalbuminuria (MAU). Among patients with JIA, microalbuminuria was detected in 7 patients (13.2%). In 42.8% of patients, an increase in the concentration of albumin in the urine of more than 20 mg / l was observed in patients with a duration of juvenile idiopathic arthritis for more than 5 years, 28.6% - in children with a disease duration of 1-3 and 3-5 years.

Thus, the analysis of the clinical variants and course of juvenile idiopathic arthritis indicates the aggressiveness and progressive nature of the course of the disease, which reflects the modern age evolution of the disease, as well as damage to internal organs, especially the kidneys, which dictates the need to find effective methods for optimizing treatment and preventing toxic effects medicines on the kidneys.

4. Conclusions

1. The duration of the course in JIA in children ranges from 3 months to 8 years, large and medium joints are more often affected - knee, ankle, wrist, elbow, hip. Persistent course was noted in 28.9% of the patients, and a progressive course- in 71%.
2. The course of the features of the articular syndrome by sex showed that the exudative component of 39% is less pronounced in boys, productive-dystrophic changes of 61% in the joints of the lower extremities predominate. In girls, exudation in the joints of the upper extremities prevailed - 85%. The average age of the patients was 7 years, X-ray was determined mainly II degree according to Steinbrokker.
3. Kidney damage in the form of nephritis was observed in 60.5%, microalbuminuria - in 13.2%, an increase in the concentration of creatinine in the blood – 68%.

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