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OUTCOMES AND PROGNOSIS IN PATIENTS WITH VARIOUS VARIANTS OF JUVENILE ARTHRITIS AFTER 10 AND MORE YEARS FROM THE BEGINNING OF THE DISEASE

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Abstract. Currently, there are studies on the evolution and outcomes of juvenile arthritis (JA) in adults. As a rule, the outcome in the group of patients suffering from long-term JA, but not yet beyond the limits of childhood and adolescence, is assessed according to the same parameters as in adult patients, with the exception of filling out childhood-specific questionnaires on functional status.

Keywords: juvenile arthritis, rheumatoid factor, DMARDs

Introduction. At the present stage of development of pediatric rheumatology, one of the urgent problems, along with issues of early diagnosis, improvement of methods for the treatment of chronic inflammatory joint diseases in children, is the study of long-term outcomes and prognosis in patients with juvenile arthritis (JA). The generally accepted concept of outcome as the end of the disease (death or recovery) is not used in chronic diseases, because they are infrequently the cause of death, and recovery is practically not observed [1]. Therefore, many authors under the term “outcome” in JA understand the patient’s condition after a certain period of time from the onset of the disease, usually at least 7–10 years [2–6]. In the absence of specific standards for describing the outcome of JA, most researchers use indicators such as clinical manifestations, functional status, laboratory parameters, and, in recent years, also indicators of quality of life [7–12, 13-25].

Currently, JA is considered as a heterogeneous group of diseases that have different clinical manifestations and a different course of the pathological process, therefore, the outcome of individual variants of the disease is not the same. A number of authors believe that differences in the outcome of the disease and prognosis directly depend on both the form of onset and age at the onset of the disease. According to others, the variant of the course of the pathological process, which changes in 1/3 of patients with JA, is more important.

Until now, the question of the activity of the disease and the possibility of forming remission in patients after 10 or more years from the onset is being discussed. Data on the state of the musculoskeletal system and the formation of serious functional disorders with a long duration of the disease are also ambiguous, although in recent years there has been a clear decrease in the number of disabled patients due to the introduction of early prescription tactics of basic anti-inflammatory drugs (DMARDs), as well as the emergence of new antirheumatic

drugs. means, for example, biological agents, for the treatment of JA. In addition, studies on the outcomes of JA present disparate information regarding the general physical development of patients, extra-articular manifestations of the disease, radiographic changes in patients with long-term chronic inflammatory joint diseases.

Currently, there are studies on the evolution and outcomes of JA in individuals who have reached adulthood [12]. As a rule, the outcome in the group of patients suffering from long-term JA, but not yet beyond the limits of childhood and adolescence, is assessed according to the same parameters as in adult patients, with the exception of filling out childhood-specific questionnaires on functional status. However, in the literature of the last 10–20 years, studies reflecting the outcome of JA in childhood are few [2,12]. The authors, as a rule, track the evolution of JA in patients in different periods, without dividing them into categories of children or adults.

All of the above served as the basis for conducting a study on the evolution of JA with a long duration of the disease within the framework of childhood, as well as the characteristics of the course of its various variants.

Purpose of the study: To assess the evolution and outcomes of JA in patients with a disease duration of 10 years or more within childhood and adolescence.

Material and methods

The work was based on observations of 96 patients with JA who were hospitalized in the Ferghana Regional Multidisciplinary Medical Center in the period from 2020–2022.

The inclusion criteria for the study were: the presence of JA (juvenile rheumatoid arthritis or juvenile chronic arthritis), age under 18 years, disease duration of 10 years or more.

The age of the children ranged from 11 to 18 years (average 14.3 ± 2.0 years), they were predominantly girls (83%). The duration of the disease ranged from 10 to 16 years (average 12.0 ± 2.0 years). All patients applied to the State Institute of Rheumatology, Russian Academy of Medical Sciences, on average 2 years after the onset of the disease.

During the formation of groups, systemic, polyarticular (RF+ and RF–) and oligoarticular variants of JA were identified, the latter having two subtypes: persistent oligoarthritis (the number of joints involved in the process did not exceed 4 throughout the disease) and oligoarthritis, spreading (5 or more affected joints) after 6 or more months from the onset of the disease.

In all variants of the disease, girls predominated (68–88%). There were no significant differences between the selected groups in terms of age at the time of the examination and the duration of the disease. At an earlier age, the first signs of the

disease appeared in children with oligoarthritis (1.8 ± 1.0 years), especially compared with patients with RF-positive polyarthritis (5.1 ± 2.8 years).

The patients included in the study were examined according to the scheme generally accepted in rheumatology. Clinical and laboratory parameters, the nature of the onset and course of the disease, the degree of activity of the process, the presence of remission, the functional and social status of patients with JA 10 years after the onset of the disease were assessed.

Results. In the majority of patients (95%), the disease manifested with arthritis from the first days. 3% of children complained of arthralgia, and subsequently developed arthritis. At the onset of the disease, almost half of the patients (41%) involved predominantly large joints in the process, and 1/3 had damage to the joints of the lower extremities. In 63% of patients, symmetrical arthritis developed at an early stage of the disease, to a greater extent this was characteristic of patients with systemic and polyarticular forms. In the same groups, the hip joints and cervical spine (CS) were involved rather early in the process (35 children).

An analysis of outcome parameters in children and adolescents suffering from JA for 10 years or more revealed that in the majority of patients who had oligoarthritis at the onset (50 children), the number of affected joints later exceeded 5 with the formation of polyarthritis (spread oligoarthritis), in the remaining children and adolescents, the articular syndrome recurred, but did not progress quantitatively (patients with persistent oligoarthritis). Polyarthritis already at an early stage of the disease had 25% of patients, among them seropositivity for the Russian Federation was noted only in 5 patients. In general, it was found that over time, all forms of JA (oligoarticular - in 82% of patients, polyarticular - in 58%, systemic - in 45%) tended to spread the articular syndrome and form a polyarticular variant of the lesion, which is consistent with the results of foreign studies. [26-40].

At the time of the examination, the majority (55%) of patients had no active arthritis, although there were functional disorders associated with previous arthritis. 43 children had signs of arthritis, but the number of inflamed joints did not exceed 4. The presence of active polyarthritis (more than 4 inflamed joints) was more typical for patients with advanced oligoarthritis and RF-positive polyarthritis.

Systemic manifestations of the disease at the onset of JA were observed in 22 children (23%). Subsequently, they recurred in 19 patients, and at the time of the study they were present only in 3 patients and were represented by individual manifestations or their combinations. Significantly more frequent were such systemic signs as fever, rash, polyadenia, hepatosplenomegaly, serositis was much less common. It should be noted that out of 76 patients with the articular form of JA, 6

had systemic signs, such as fever and polyadenia, that appeared during the course of the disease and reflected the activity of the pathological process [41-55].

Of other extra-articular manifestations, attention should be paid to the pathology of the organs of vision. During the course of the disease, eye damage was diagnosed by an ophthalmologist in 37% of patients (36 children), mainly in the form of uveitis (35 people) and was interpreted as a manifestation of the underlying disease. It occurred in oligoarthritis (persistent and spreading) and in RF seronegative polyarthritis (47–55% of patients). Eye damage appeared on average after 5.7 ± 3.8 years from the onset of the disease. There were observations of the development of uveitis after a long period from the onset of arthritis (maximum after 11 years). It should be noted that uveitis was not detected in any patient with RF-positive polyarthritis or a systemic form of the disease. Uveitis was usually chronic and bilateral. At the time of examination, in most patients, the inflammatory process in the eyes was inactive or in remission. Complications (cataract, glaucoma, synechia, etc.) were registered in 28 people. Cataract in 8 patients with the systemic form of JA was associated with the use of GC drugs.

As for other extra-articular manifestations of the disease, there were no significant deviations from the internal organs in patients. The most serious complication of JA, secondary amyloidosis, was diagnosed in 2 adolescent boys with a systemic form.

Assessing the condition of patients 10 years after the onset of the disease, it should be noted that more than half of the patients still had disease activity. In 47% of patients, the pathological process recurred and progressed, 24% showed stabilization. About 1/3 of the children (29%) were in remission, with half of them continuing to receive antirheumatic drugs.

We drew attention to the fact that half of the children (55%) had remissions during the course of the disease, including 20 patients in the absence of any treatment. Remissions were at different times from the debut (from 1 year to 12 years), and their duration varied from 1 year to 6.5 years (average 4.0 ± 3.0 years). Complete remission (in the absence of antirheumatic treatment) was significantly more often recorded in patients with persistent oligoarthritis (30.4%) than in patients with other forms of JA. Drug remission, which occurred in a third (34%) of children with JA, in most of them (89%) was associated with the intake of basic drugs (more often methotrexate) and occurred on average after 3.2 ± 2.8 years from the start of this type of therapy (from 6 months to 8.5 years). The average duration of remission during treatment was 3.0 ± 2.0 years (from 1 to 7 years). There were no significant differences in the frequency of drug-induced remission in different types of JA.

When examining patients 10 years after the onset of the disease, it was stated that the presence of persistent activity or its absence did not depend on either the form of the onset or the nature of the course of JA ($p>0.05$). In the group of patients with persistent activity at the time of the examination, patients with a low (I and II) degree of activity (84%) prevailed. Only in 16% of children the disease continued to be highly active. The minimum activity of the disease was significantly more often determined in patients with oligoarthritis compared with systemic and polyarticular forms of JA.

Positive RF at the time of examination was observed in 4 patients (4%) in titers 1/40–1/160. These were patients with spreading oligoarthritis - 2, polyarthritis - 1, systemic form - 1 patient. During the course of the disease RF was registered in 22 patients (23%). ANF during the course of the disease was detected in 55 children, and significantly more often in patients with advanced oligoarthritis (47%) and seronegative polyarthritis (22%). After 10 years or more from the onset of JA, ANF was detected in 16% of children (in titers from 1/20 to 1/160). At the same time, there was a significant relationship between its presence and eye damage, but there was no correlation with the form of JA.

An analysis of the x-ray picture showed that one third of the children (33%) had stage I or minimal x-ray changes in the joints, among which patients with persistent oligoarthritis predominated. Stage II was detected in almost a quarter of patients (25%). The most pronounced destructive process in the area of the joints (stages III and IV) was noted in 42% of patients, more often with a systemic form and RF-positive polyarthritis. Radiographically confirmed ankylosis, predominantly of the wrist and SHOP joints, was diagnosed in 17% of patients.

In 35% of patients with JA, the course of arthritis led to the development of aseptic necrosis. The most common localization in the vast majority of patients (91%) was the heads of the femur, mainly in patients with systemic JA.

When studying the x-ray picture of the disease with a long course of JA, attention was paid to the signs of osteoarthritis (narrowing of the joint space + the presence of osteophytes) in 68% of children. They were observed mainly in the most affected joints and were regarded by us as secondary against the background of a long-term ongoing inflammatory process. They were more often detected in patients with a systemic form and RF-positive polyarthritis. The presence of signs of secondary osteoarthritis in patients had a direct relationship with the severity of destructive changes in the joints ($p<0.02$), but did not correlate with the degree of functional disorders in them ($R=0.02$, $p=0.7$).

Assessment of the functional state of children and adolescents on the Steinbroker scale showed that the functional ability of most of them was preserved

(FC I and II: 34% and 41.6%). In 23% of patients, it was only possible to perform normal activities or self-care (FC III), and only 1 child was limited to a wheelchair at the time of inclusion in the study. The most functionally intact patients were those with persistent oligoarthritis, and the most pronounced disorders were in patients with polyarticular and systemic forms of JA, but this was not statistically significant.

When filling out the Russian version of the CHAQ questionnaire, 20% of patients noted that they did not have functional disorders (CHAQ=0), and most of them were patients with persistent oligoarthritis. 19% of children had minimal impairments (CHAQ=0.1–0.5), a third had a moderate degree of PE (CHAQ=0.6–1.5). Significant functional limitations (CHAQ>1.5) were experienced by 28% of patients, among whom patients with systemic JA predominated. The data obtained indicate that among patients with the onset oligoarticular form, the most favorable course and outcome were in patients with persistent oligoarthritis (average CHAQ = 0.3 points), while the course and outcome of the disease in patients with advanced oligoarthritis (average CHAQ=0.8 points) approached polyarticular (mean CHAQ=1.0 points) and systemic (mean CHAQ=1.3 points) forms of JA, being more severe.

76% of children (73 patients) were recognized as disabled due to the disease. In the vast majority, this was due to severe destructive changes in the joints, which led to pronounced functional disorders (69 people). 4 children were disabled due to the state of the organs of vision.

Despite the duration of the disease, the physical development of more than half of the patients included in the study was age-appropriate. However, 48% of children lagged behind their peers or differed significantly from them in appearance due to disproportionate development. Lagging in physical development was more common in patients with polyarticular and systemic forms of the disease, but did not differ statistically from patients with other forms of JA. At the same time, with persistent oligoarthritis, the physical development of all patients significantly more often corresponded to age, in contrast to other groups.

73% of children studied in a regular school on a par with their peers, although some of them studied according to an individual program. 26% of children were forced to study at home or attend a special school, mostly suffering from a systemic form or seropositive polyarthritis.

Conclusion. Thus, as a result of the study, we found that after 10 years or more from the onset of JA, 71% of children and adolescents had inflammatory activity of the disease, but its severity was low (grades I and II), especially in patients with oligoarthritis. Over time, all forms of JA tended to spread the articular syndrome and form a polyarticular variant of the lesion. Polyarticular and systemic forms of JA on

debut were the most unfavorable in terms of prognosis (presence of disease activity, extra-articular manifestations, amyloidosis), radiological (stages III–IV) and functional (FC III–IV, CHAQ >1.5 points) outcomes. Among patients with the onset oligoarticular form, the most favorable course and outcome were those with a persistent variant, while the course and outcome of the disease in patients with advanced oligoarthritis approached polyarticular and systemic forms of JA. The foregoing indicates that certain categories of patients require careful monitoring and active treatment from the early stages of the disease in order to avoid serious disorders of the musculoskeletal system that affect the patient's physical and social adaptation in the future.

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