

CLINICAL AND INSTRUMENTAL CHARACTERISTICS OF JUVENILE CHRONIC ARTHRITIS EVOLUTION

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The purpose of the study was to investigate the clinical symptoms and evolution of juvenile chronic arthritis (JCA) at different stages of its development. 39 children with duration of JCA from 6 months to 5 years in age from 2 to 18 years were examined. All patients underwent clinical examination, indicators of acute phase of inflammation (CRP, sialic acid, seromucoid, glycoproteins), rheumatoid factor, circulating immune complexes, complement, instrumental methods (X-ray and ultrasound, capillaroscopy of nail bed) were evaluated. Activity of the disease was estimated by disease activity score (DAS28). Statistically was determined the relative value (P). It was found that the disease started with monoarthritis (63,37%). In the future, in half of the patients was formed oligoarthritis with damaging of large and medium-sized joints (68,25%). In the majority of surveyed disease occurred against the backdrop of the minimal activity of the inflammatory process. On the stages of evolution recurrence of arthritis were observed in one third of children. If duration of the sickness is more than 5 years, it has become less frequent, than in previous years. The absence of clinical and radiographic manifestations of JCA after the abolition of medical treatment within one year, became the basis for the assumption that the disease remission, which was on the third year of the disease 25,93%, on the fourth – 33,33%, on the fifth – 36,36%. The absence of radiographic signs of bone destruction, disability of patients allows interpreting JCA as a positive option of chronic juvenile idiopathic arthritis.

KEY WORDS: juvenile chronic arthritis, juvenile idiopathic arthritis, children

КЛІНІКО-ІНСТРУМЕНТАЛЬНА ХАРАКТЕРИСТИКА ЕВОЛЮЦІЇ ЮВЕНІЛЬНОГО ХРОНІЧНОГО АРТРИТУ

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Метою дослідження було вивчення клінічної симптоматики та еволюції ювенільного хронічного артрити (ЮХА) на різних етапах розвитку. Обстежено 39 дітей з ЮХА тривалістю від 6 місяців до 5 років, віком від 2 до 18 років. У всіх хворих проводили клінічне обстеження, оцінювалися показники гострої фази запалення (СРБ, сіалові кислоти, серомукоїд, глікопротеїди), ревматоїдний фактор, циркулюючі імунні комплекси, комплемент, застосовувалися інструментальні методи (рентгенологічне та ультразвукове дослідження, капіляроскопія нігтьового ложа). Проводилась оцінка активності хвороби disease activity score (DAS28). Статистично визначали відносну величину (P). Встановлено, що захворювання нерідко починалося з моноартриту (63,37%). Надалі у половини хворих формувався олігоартрит з пошкодженням великих і середніх суглобів (68,25%). У більшості обстежених перебіг хвороби був на фоні мінімальної активності запального процесу. На етапах еволюції рецидиви артрити спостерігалися у третини дітей. При тривалості хвороби 5 років вони стали менш частими, ніж у попередні роки. Відсутність клінічних та рентгенологічних проявів ЮХА після відміни медикаментозного лікування протягом одного року стала підставою для трактування клініко-лабораторної ремісії захворювання, яка склала на третьому році хвороби 25,93%, четвертому – 33,33%, п'ятому – 36,36%. Відсутність рентгенологічних ознак деструкції кісток, інвалідизації хворих трактує ЮХА, як певний хронічний позитивний варіант ювенільного ідіопатичного артрити.

КЛЮЧОВІ СЛОВА: ювенільний хронічний артрит, ювенільний ідіопатичний артрит, діти

КЛИНИКО-ИНСТРУМЕНТАЛЬНАЯ ХАРАКТЕРИСТИКА ЭВОЛЮЦИИ ЮВЕНИЛЬНОГО ХРОНИЧЕСКОГО АРТРИТА

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Целью исследования было изучение клинической симптоматики и эволюции ювенильного хронического артрита (ЮХА) на разных этапах развития. Обследовано 39 детей с ЮХА продолжительностью болезни от 6 месяцев до 5 лет, в возрасте от 2 до 18 лет. Всем больным проводили клиническое обследование, оценивали показатели острой фазы воспаления (СРБ, сиаловые кислоты, серомукоид, гликопротеиды), ревматоидный фактор, циркулирующие иммунные комплексы, комплемент, применялись инструментальные методы (рентгенологическое и ультразвуковое исследование, капилляроскопия ногтевого ложа). Проводилась оценка активности болезни disease activity score (DAS28). Статистически определяли относительную величину (P). Установлено, что заболевание начиналось с моноартрита (63,37 %). В дальнейшем у половины больных формировался олигоартрит с повреждением крупных и средних суставов (68,25 %). У большинства обследованных болезнь протекала на фоне минимальной активности воспалительного процесса. На этапах эволюции рецидивы артрита наблюдались у трети детей. При продолжительности болезни более 5 лет они стали менее частыми, чем в предыдущие годы. Отсутствие клинических и рентгенологических проявлений ЮХА после отмены медикаментозного лечения в течение одного года стала основанием для предположения о ремиссии заболевания, которая составила на третьем году болезни 25,93%, четвертом – 33,33 %, пятом – 36,36 %. Отсутствие рентгенологических признаков деструкции костей, инвалидизации больных позволяет трактовать ЮХА, как некий хронический положительный вариант ювенильного идиопатического артрита.

КЛЮЧЕВЫЕ СЛОВА: ювенильный хронический артрит, ювенильный идиопатический артрит, дети

INTRODUCTION

Juvenile idiopathic arthritis (JIA, a term was introduced in 1997 by EULAR) is a heterogeneous group of diseases that mainly tends to progressive flow and affects the quality of life of a sick child [1–4]. An important feature is their destructive joint damage that determine prognosis [1, 5–6]. There are three clinical variants of JIA debut: systemic, polyarticular and oligoarticular. Among the latest subtypes were detailed persistent (with damaging in less than 5 joints throughout the disease) and common (arthritis develops in more than 4 joints after 6 months of illness), also psoriatic arthritis, arthritis associated with enthesitis, other arthritis [7–9].

In initial stages of JIA different options, clinical symptoms in the further evolution so often characterized by considerable similarity of symptoms, making it difficult not only for diagnose, but also for right treatment [2, 5, 10]. Especially in this respect stands juvenile chronic arthritis (JCA). This term is used since 1977 by EULAR in case when it is impossible to establish a particular nosology, or when it is possible to predict that disease is in the stage of

formation [5, 7]. However, JCA is not foreseen in the existing part of JIA terminology.

OBJECTIVE

The purpose of the study is to improving diagnosis and prognosis of JCA based on the examination of the evolution of symptoms and disease in various stages of development.

MATERIALS AND METHODS

In clinic SI «Institute of children and adolescents health care of the NAMSU» 39 children with JCA lasting from 6 months to 5 years and aged from 2 to 18 years were examined. The average age was $9,85 \pm 0,67$ years. Duration of illness was up to one year in 20,51 % of cases, two years – 25,64 %, three years – 30,77 %, four years – 7,69 %, five years – 17,95 %. Among patients with JCA were more females (53,85 %).

Diagnosis was guided by X International Classification, unified clinical protocols of medical care for children with juvenile arthritis No 832 from 22.10.2012 approved by the Ministry of Health of Ukraine, classification of juvenile idiopathic arthritis (ILAR; 1997, 2001). All sick children were examined including clinical, biochemical, immunological,

radiological, ultrasonic methods. Activity of disease was assessed by disease activity score – DAS28, radiographic signs in joints by Steinbrocker scale.

Changes of articular apparatus structures were determined by ultrasound (US) according to developed protocols. All patients were analyzed by acute phase parameters (CRP, sialic acid seromuroid, glycoproteins), rheumatoid factor (RF), circulating immune complexes (CIC) (screening test), complement (by Chudomels in modification of Kondrashova N. I., 1974).

State of microcirculation in children with JCA was determined by capillaroscopy of nail bed. The method was performed in the morning before a meal in ambient temperature near 20–22 °C by capillaroscope M-70A with a magnification in 28 times that allowing to measure the object with an accuracy of 0,05 mm.

All patients during active manifestation of JCA received nonsteroidal anti-inflammatory drugs (diclofenac 2,5–3 mg/kg/day). 34,12 % of patients received glucocorticoids intraarticular. 72,50 % persons appointed by the disease-modifying drugs, including sulfasalazine 30 mg/kg/day.

The study was conducted during the initial investigation of patients in the clinic SI «Institute of children and adolescents health care of the NAMSU» and in the dynamics within five years of the disease.

Statistical analysis of the results was carried out by using the application Statgrafics-5 with the definition of relative value (P) of investigated characteristics.

RESULTS AND DISCUSSION

Debut of articular manifestations in children has been presented mostly by monoarticular lesions (63,37 %). Changes were observed mainly in large and medium-sized joints. The most vulnerable were joints of the lower extremities – knees (60,93 %), significantly lower – shins (9,75 %) and hipbones (9,75 %). Sometimes can be affected radiocarpal joints (7,31 %) and small joints of hands (2,43 %). Twoness of involving joints was observed in 21,93 % of patients. Articular syndrome was characterized by swelling of the joints with deformation (73,12 %), pain during active (39,77 %) and passive movements (43,87 %).

Noteworthy was the presence of morning stiffness in a small proportion of patients

(17,06 %), which was mainly short-term. At 4,87 % of patients was diagnosed by regional hypomyotrophy. Mostly, it was manifested in children with a history of illness for more than 15 months. The functional ability of joints suffering mainly on the background of pain. However, even with a steady arthritis limits of movement had little expression and were easily reversible. Given the potentials impact of connective tissue dysplasia to the appearance and evolution of the disease, which has been studied, each patient was determined by signs of hypermobility of joints (GMJ). It was found that it was observed in 30,77 % of children. It was revealed that GMJ prevailed in the age group 6-15 years (73,12 %) and limitation of movement was absent in the presence of GMJ.

According to the assessment of pathological process by DAS28 activity index low activity was diagnosed in 17,06 %, average – in 15,60 % of patients. In remaining patients process wasn't active.

Acute phase indicators including ESR and CRP were mostly normal (82,87 % and 78,00 % respectively), elevated in patients with polyarthritis and olihoartrytom (14,62 % and 19,50 % respectively). Indicators of RF, CIC and complement didn't have deviations from normal.

According to ultrasound investigation signs of synovitis were detected in 78,00 %. Synovitis was determined by the presence of clinical signs of arthritis. In patients with a longer history of pathological process were detected changes of synovial membrane in the form of thickening and proliferation (12,18 % and 14,62 % respectively).

Radiographic changes in the joints at the end of the first year were found in the half of patients. Mainly it was defined as epiphyseal osteoporosis (49,68 %).

In JCA vascular changes (81,32 %) were found in a small number of vessels in the form of tortuosity, uneven caliber, occasionally - as ischemic zones and single aneurysms (14,75 %). Intravascular disorders (58,44 %) were characterized by the rise mainly in venules with slowing of blood flow and fine-grained aggregation of red blood cells. Perivascular background was involved in the pathological process in 24,91 % of cases as a pale color. Microcirculatory disorders were nonstable, they were decreased with elongation of disease duration and remission and then appeared in the exacerbation of the pathological process.

JCA in children is characterized by propensity to recurrence of the pathological process. Signs of re-arthritis in stages of the evolution of the disease remained shorter than in the debut and developed in previously damaged as well as in healthy joints. Relapses of arthritis were observed in one third of children and were more recorded in the second and third years of the disease (42,11 % and 40,74 %). In five year follow-up it has become less frequent than in previous years.

On stages of an evolution of the articular syndrome took place a shift in the ratio of the amount of joint damage (monooligopolyarthritis) to oligoarticular defeats. At the end of the observation significant impairment of joint function was not occurred.

Analysis of clinical symptoms and laboratory and instrumental data in the second year of the disease showed that against a background of minimal activity of the inflammatory process in the majority of patients still have been defeat of large and medium-sized joints (68,25 %). Radiological changes at this stage of the disease were detected in 57,89 % of children and manifested as osteoporosis.

In earlier studies of Lebet's I. S. was shown that the clinical course of JCA is characterized by low activity of the inflammatory process, monooligoarticular lesions, arthritis of the knees and ankle joints that persists for a long period of time (4 months or more), relapsing of disease without progression of articular syndrome [11]. In article of Salugina S. A. [12] presents clinical and radiological signs of JCA in children, who are in general agreement with our data. Especially it concerns such important features as a low frequency of symmetrical lesions of small joints, muscular atrophy, morning stiffness and the presence of osteoporosis in the majority of patients. We have found that despite the relapses of JCA on the third or fourth year, in third part of patients was presented complete regression of clinical and ultrasound changes in the joints, and in the five-year history in 54,55 % of patients. However, radiological signs of the disease (osteoporosis) were remained respectively in

37,04 % and 18,18 % of patients. The absence of clinical and radiographic manifestations of JCA after the abolition of medical treatment within one year became the basis for the interpretation of disease remission, which was on the third year of the disease 25,93 %, on the fourth – 33,33%, on the fifth – 36,36 %.

CONCLUSIONS

Despite unknown and possibly different triggers that contribute the development of chronic inflammation in the joints, there are certain patterns in the manifestations of JCA (in the structure of JIA). It was established that the disease is characterized by monooligoarticular destruction of large and medium-sized joints, usually knees and shins with moderately pronounced signs of long-term arthritis. In more than 2/3 of children was found recurrent arthritis on the different stages of the evolution of the pathological process, but mostly in the second and third year of the disease often with damaging of previously healthy joints.

However, most children with JCA have favorable prognosis with the development of resistant or less long-term remission with complete regression of the articular syndrome. At a certain similarity between the clinical manifestations with JRA JCA is distinguished by the absence of symmetry defeat of small joints, bursitis, lesions of the eyes, morning stiffness. Radiographic changes in the joints at JCA less serious than in the JRA. This also applies to deviations in immunological parameters in such patients. JCA is a definite positive chronic variant of JRA in the progress and complications.

PROSPECTS FOR FUTURE STUDIES

The study allowed identifying and describing the clinical and paraclinical manifestations of JCA in children. A promising direction is depth studying of metabolic and immunological changes during JCA and identifying relationships between them. Further research in that direction will help to improve approaches to the treatment of patients with this pathology.

REFERENCES

1. Alekseyeva Ye. I. Yuvenil'nyy idiopatcheskiy artrit: klinicheskaya kartina, diagnostika, lecheniye / Ye. I. Alekseyeva // *Voprosy sovremennoy pediatrii*. – 2015. – № 1. – S. 78–94.
2. Karateyev D. Ye. O klassifikatsii revmatoidnogo artrita / D. Ye. Karateyev, Yu. A. Olyunin // *Nauchno-prakticheskaya revmatologiya*. – 2008. – № 1. – S. 5–16.

3. Martini A. Systemic juvenile idiopathic arthritis / A. Martini // *Autoimmun. Rev.* – 2012. – № 12. – P. 56–59.
4. Marzan K. A. B. Early juvenile idiopathic arthritis / K. A. B. Marzan, B. Shaham // *Rheum. Dis. Clin. North Am.* – 2012. – № 38. – P. 355–372.
5. Bentsa T. Yuvenil'nyye khronicheskiye artrity / T. Bentsa // *Liki Ukraïni.* – 2005. – № 4. – S. 27–30.
6. Wallace C. A. American College of Rheumatology provisional criteria for defining clinical inactive disease in select categories of juvenile idiopathic arthritis / C. A. Wallace, E. H. Giannini, B. Huang // *Arthritis Care Res. (Hoboken).* – 2011. – № 63. – P. 929–936.
7. Baranov A. A. Yuvenil'nyy artrit: klinicheskiye rekomendatsii dlya pediatrov / A. A. Baranov, Ye. I. Alekseyeva. – M.: *Pediatr*, 2013. – 120 s.
8. Berezhniy V. V. Kharakteristika klinichnogo perebigu revmatoïdnogo artritu na suchasnomu yetapí / V. V. Berezhniy, T. V. Marushko // *Zdorov'ye zhenshchiny.* – 2005. – № 4. – S. 172–175.
9. Beukelman T. College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features / T. Beukelman, N. M. Patkar, K. G. Saag // *Arthritis Care Res. (Hoboken).* – 2011. – № 63. – P. 465–482.
10. Otten M. H. Efficacy of biological agents in juvenile idiopathic arthritis: a systematic review using indirect comparisons / M. H. Otten, J. Anink, S. Spronk // *Ann. Rheum. Dis.* – 2013. – № 72. – P. 1806–1812.
11. Lebedev I. S. Diagnosticheskiye i prognosticheskiye algoritmy yuvenil'nogo khronicheskogo i reaktivnogo artrita // *Okhrana zdorov'ya detey i podrostkov: Resp. mezhved. sb.* – K., 1996. – Vyp. 25. – S. 26–29.
12. Salugina S. O. Sovremennyye podkhody k diagnostike yuvenil'nykh artritov / S. O. Salugina, N. N. Kuz'mina, N. V. Fillipova // *Prakticheskaya revmatologiya.* – 2010. – № 3. – S. 65–72.