

THE DIAGNOSTIC VALUE OF ANTIBODIES TO MODIFIED CITRULLINATED VIMENTIN IN CHILDREN WITH JUVENILE ARTHRITIS

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Abstract: The article presents the study results of the value of Anti-MCV in children with juvenile arthritis, depending on the variant of the disease. An analysis of obtained results reveal that in children with juvenile arthritis, Anti-MCV indicates the likelihood of the joint syndrome formation, that frequently leads to the development of significant functional insufficiency of the joints, which is the justification for the early appointment of active, often aggressive therapy in order to prevent disability of the patient. The level of Anti-MCV can be as a basis for the using of this indicator in monitoring activity and assessing the effectiveness of treatment.

Keywords: children, juvenile arthritis, antibodies to modified citrullinated vimentin.

Background

Diagnosis of juvenile arthritis (JA) presents certain difficulties, especially in the early stages of the disease due to the lack of modern diagnostic criteria and specific laboratory tests. The number of laboratory tests that have high sensitivity and specificity which help in the early recognition of a variant of JA in pediatric rheumatology is limited [2, 4, 5, 10, 11, 12, 16,18].

In recent years, a certain diagnostic importance has been attached to new immunological indicators– antibodies to cyclic citrullinated peptide (Anti-CCP) and antibodies to modified citrullinated vimentin (Anti-MCV) [1, 2, 3, 6, 14, 15, 17].

Determination of Anti-MCV (anti-Sa antibodies) is one of the most promising (in diagnostic and prognostic terms) tests in patients with rheumatoid arthritis (RA). Anti-MCV are antibodies that interact with synthetic peptides containing citrulline [1,7, 8, 9, 15, 16, 19, 20].

The literature discusses the role of Anti-MCV for the diagnosis of RA in adults as a new immunological marker along with RF and Anti-CCP, especially in the early stages of the disease [20].

According to the literature, Anti-MCV has a sufficiently high sensitivity (53.7-82.0%) and specificity (89.8-98.7%) for the diagnosis of RA exceeding these indicators for Anti-CCP. Moreover, the specificity of Anti-MCV increases and exceeds that for rheumatoid factor (RF) when using a higher level of “cut off” [4,7,8, 16,17, 20].

The detection of antibodies to modified citrullinated vimentin and RF significantly increases the probability of a diagnosis of rheumatoid arthritis [1, 3, 8, 11, 16, 18].

Based on the above, the study of the role of Anti-MCV in children with JA is of great importance.

The aim of our study was to determine the concentration and frequency of increase in the level of Anti-MCV and its diagnostic significance in children with JA.

Research materials and methods

The study included 85 children who were on inpatient treatment in the Department of Cardiorheumatology of the RSSPMC of Pediatrics. The age of children were from 2 to 18 years (med. 8, 5 + 1, 1 years). The duration of the disease varied from 6 months to 15.5 years (average 5.4+0.9 years).

Anti-MCV was determined in 85 patients with JA (57-girls, 38-boys). To determine the differences in the level of Anti-MCV between the variants of JA, the children were divided into 2 groups depending on the variant of the disease:

- Group 1 – 37 (43.5%) patients with the articular variant of JA;

- Group 2 – 48 (56.5%) patients with systemic JA (SoJA).

Statistical processing of the results was carried out using the software package for IBM PC "Statistica 7.0", "BIOSTAT". To describe the nature of the distribution of quantitative features, standard methods of variational statistics were used with the determination of the arithmetic mean (M), the mean (standard) quadratic deviation (σ), for an incorrect distribution – median (Me) and interquartile range (IR). The reliability of the differences between the groups when comparing quantitative parameters was assessed using the Student's T-test. If the significance level of p was less than 0.05 ($p < 0.05$), the differences were considered statistically significant.

Results and discussion

Vimentin, usually performing a structural role, is found in large quantities in the synovial membrane of the joints. Under the influence of inflammatory mediators, vimentin undergoes citrullination, a process in which the amino acid arginine in vimentin is converted into citrulline. Citrullinated vimentin acts as an antigen for autoantibodies in rheumatoid arthritis [1, 3, 4].

A study of the frequency of elevated Anti-MCV levels in children with JA showed that an increased Anti-MCV levels were detected in 12 (32.4%) patients with the articular variant of JA, which was 2.6 times more common than in children with SoJA ($p \leq 0.01$) (Fig.1).

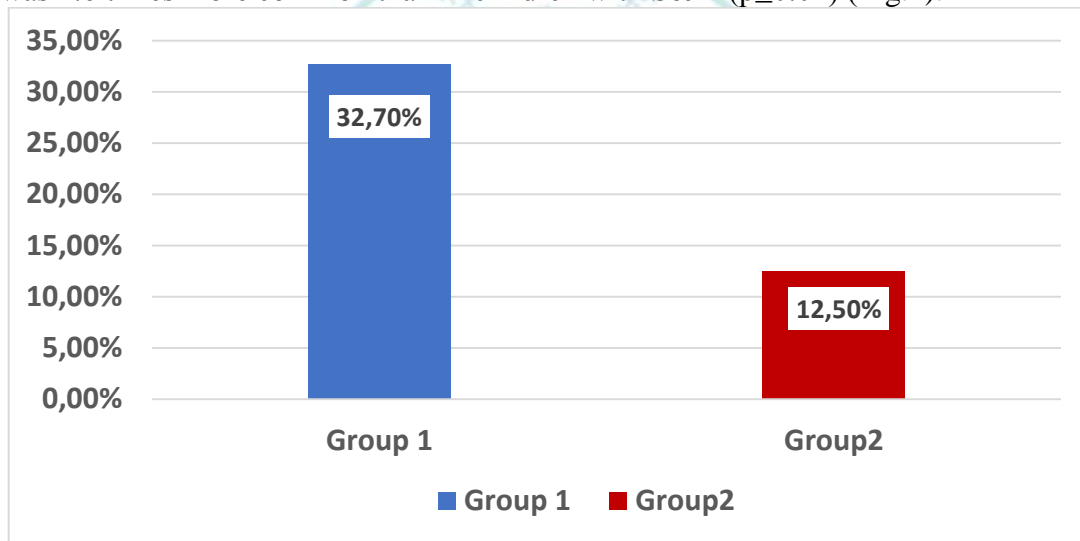


Fig.1. The number of patients (%) with a high level of Anti-MCV, depending on the variant of JA.

Significantly more often in RF positive patients than in RF negative ones ($p=0.001$), elevated levels of Anti-MCV were detected.

The concentration of Anti-MCV in the serum in the articular variant of JA ranged from 1.7 to 413.2 units/ml and its average was 39.4 ± 2.8 units/ml. In contrast, in children with SoJA, the levels of Anti-MCV in the serum were much lower and the fluctuations ranged from 0.8 to 30.5 units/ml. At the same time, its average was 7.1 ± 0.5 units/ml ($p < 0.001$) (Table 1).

An average concentration of Anti-MCV in children with JA, depending on the variant of the disease

| Indicator | Group 1 | Group 2 | p |
|--------------------|----------------|---------------|----------|
| Anti-MCV, units/ml | $39,4 \pm 2,8$ | $7,1 \pm 0,5$ | $<0,001$ |

Note: p - accuracy of the indicators between the compared groups

The presence of Anti-MCV is associated with the development of destructive changes in the joints and rapid progression of JA. The Anti-MCV concentration more accurately reflects the activity of the disease. To assess the activity of the disease, the indicators of each patient were analyzed separately [4, 7, 11, 17, 20].

The study of the antibodies level in patients depending on the variant of the disease showed that 6 (16.2%) children with the articular variant of JA had a high level of Anti-MCV (more than 30

units / ml) 5-fold exceeding the standard values, the 9-fold increase was seen in 1 (2.7%) patient and 14-fold in another (2.7%), while the rest patients had a low content of (20-30 U/ml) ($p < 0.001$). The overwhelming majority of patients with the articular variant had a low level of Anti-MCV in the serum. As the results of the study showed, both the titers of Anti-MCV concentration and the frequency of their increase are higher in children with the articular variant of disease compared with the SoJA, which indicate the presence of destructive changes in the joints and the progression of JA.

Therefore, Anti-MCV indicates the probability of joint syndrome formation, which most often leads to the development of significant functional insufficiency of the joints, which is the reason for the early appointment of active, often aggressive therapy in order to prevent disability of the patient. The level of Anti-MCV can be an indicator for monitoring activity and evaluating the effectiveness of treatment.

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