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Research Article

The Frequency of Detection of Antibodies to Citrullinated Peptides (Anti-CCP and Anti-MCV) in Patients with Juvenile Idiopathic Arthritis and Clinical Characteristics of Seropositive Patients

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Abstract

The data on the frequency of detection of antibodies to cyclic citrullinated peptide and modified citrullinated vimentin in children with juvenile idiopathic arthritis are presented; clinical characteristics of seropositive patients are given. It was shown that in total antibodies to citrullinated peptides were detected in 25.4% of cases. More than 70% of patients seropositive for antibodies to cyclic citrullinated peptide and modified citrullinated vimentin developed symmetric polyarthritis at the time of examination, regardless of the type of disease onset.

Keywords: *Juvenile Idiopathic Arthritis; Antibodies to Cyclic Citrullinated Peptide (Anti-CCP); Antibodies to Modified Citrullinated Vimentin (Anti-MCV)*

Introduction

Juvenile idiopathic arthritis (JIA) is a severe chronic progressive disease of children and adolescents that arose before age of 16 years, with an unclear etiology and pathogenesis, which manifests itself as a predominant lesion of the joints, is often accompanied by extra-articular manifestations, disrupts the growth and development of the child [1-3].

Today, there is no doubt that various immunological mechanisms are involved in the formation of chronic inflammation in different types of JIA. At the same time, the diagnosis of JIA is difficult, especially in the early stages of the disease, due to the lack of both modern diagnostic criteria and reliable laboratory tests, including immunological ones, with high sensitivity and specificity [4,5].

Currently, in JIA, a certain diagnostic value is attached to antibodies against Cyclic Citrullinated Peptides (anti-CCP) and antibodies to Mutated Citrullinated vimentin (anti-MCV), the detection of which has already become the gold standard for early rheumatoid arthritis diagnosis for adult patients [5-8].

The results of foreign studies on the frequency of detection of these autoantibodies and their clinical significance in children with JIA are rare and extremely contradictory, while in Russia there are single cases of such studies.

Aim of the Study

The aim of this study is to determine the frequency of detection of antibodies to citrullinated peptides and their clinical significance in various clinical variants of juvenile idiopathic arthritis.

Materials and Methods

The study was conducted on the basis of the specialized department of cardiology and rheumatology of the Chelyabinsk Regional Children's Clinical Hospital. The study included a continuous sample of 67 sick children with an established diagnosis of JIA, of which 22 were males and 45 were females, aged from 1 to 17 years.

In accordance with the classification criteria for JIA (ILAR, 2001) [9], were identified 3 groups of patients depending on the type of disease onset: systemic, oligoarticular and polyarticular (22, 25 and 20 people, respectively).

Serological examination consisted in the determination of IgG antibodies to CCP and to MCV by indirect enzyme-linked immunosorbent assay (ELISA) in blood serum. For this, the kits of reagents "Anti-CCP" and "Anti-MCV" (Orgentec, Germany) were used. In accordance with the manufacturer's recommendations, an antibody concentration ≥ 20 U/ml was considered a positive result for detecting antibodies to CCP and MCV.

Statistical analysis of the research results was carried out using both parametric and nonparametric methods.

Results and Discussion

In our study, it was found that the detection rates of anti-CCP and anti-MCV in children with JIA were 15 and 16%. It should be noted that 4 girls showed simultaneous detection of both anti-CCP and anti-MCV. Thus, in total, antibodies to citrullinated peptides were detected in 17 (25.4%) patients with JIA. In addition, when analyzing the case histories of these patients, it was found that 12 of them (70.6%) at the time of examination had formed polyarthritis (damage to more than 4 joints), regardless of how JIA debuted. The data on the distribution of seropositive antibodies to citrullinated peptides in JIA patients, depending on the type of disease onset, are presented in table 1.

JIA and its options for debut	Number of seropositive patients	
	n	%
JIA (n = 67) Including	17	25.4
System variant (n = 22) Including:	4	18.2
Oligoarthritis (n = 6)	-	-
Polyarthritis (n = 16)	4	25
Polyarticular variant (n = 20)	6	30
Oligoarticular variant (n = 25) Including:	7	28
Persistent (n = 20)	5	25
Widespread (n = 5)	2	40

Table 1: *Distribution of seropositive for antibodies to citrullinated peptides in JIA patients depending on the type of disease onset.*

Considering that among patients seropositive to citrullinated peptides, patients with formed polyarthritis predominated, we decided to compare this group of children with the group of patients who also have polyarthritis, but seronegative for anti-CCP and anti-MCV (29 people).

Table 2 shows the distribution of patients in the study groups depending on gender, age of the child, age of onset and duration of the disease.

As can be seen from table 2, these characteristics in the compared groups were comparable to each other. Both in one and in the other group, females predominated, the average age of patients at the time of examination was 10 years. The age of onset of clinical manifestations, as well as the duration of the disease in the compared groups, averaged 5 years.

		Number of Patients				p
	Seropositive (n = 12)		Seronegative (n = 29			
	n	%	n	%		
Sex	Female	11	91.7	20	69	0.25
	Male	1	8.3	9	31	
Child's age (M ± δ, years)		9.5 ± 4.4		10.6 ± 4.2		0.57
Debut age (M ± δ, years)		5.04 ± 4.2		5.4 ± 4.4		0.81
Duration of the disease (M ± δ, years)		4.2 ± 4.03		5.05 ± 4.8		0.59

Table 2: *Distribution of JIA patients in the compared groups depending on gender, age of the child, age of onset and duration of the disease.*

Further, we decided to analyze in these groups the data of family history of diseases of a rheumatic nature, including rheumatoid arthritis (RA) (Table 3).

	Number of Patients				p
	Seropositive (n = 12)		Seronegative (n = 29)		
	n	%	n	%	
Diseases of a rheumatic nature, including:	5	41.7	10	34.5	0.73
RA	3	60	7	70	1.0

Table 3: *Diseases of a rheumatic nature according to family history in the compared groups.*

From the above data, it follows that statistically significant differences in the analysis of family history data for diseases of a rheumatic nature, including RA, were not found in the compared groups of children.

The characteristics of the articular syndrome in the compared groups are presented in table 4.

Characteristics of the articular syndrome		Number of Patients				p
	Seropositive (n = 12)		Seronegative (n = 29)			
	n	%	n	%		
Activity	I	9	75	11	38	0.07
	II	2	16.7	11	38	0.34
	III	1	8.3	7	24	0.47
Functional joint disorder	I	2	16.7	4	13.8	1.005
	II	7	58.3	24	82.8	0.21
	III	3	25	1	3.4	0.12
Radiological stage	I	5	41.7	15	51.7	0.81
	II	4	33.3	10	34.5	1.005
	III	2	16.7	4	13.8	0.8
	IV	1	8.3	-	-	0.64
Lesion of small joints of the hands in the opening		9	75	21	72	0.83
RF		2	16.7	5	17.2	0.68
Symmetry of arthritis		12	100	16	55	0.01
Contractions		11	91.7	17	58.6	0.08

Table 4: *Characteristics of the articular syndrome in the compared groups of children with JIA.*

As can be seen from table 4, we also did not find significant differences in most characteristics of polyarticular articular syndrome in the compared groups. Regardless of the presence of autoantibodies to citrullinated peptides, the disease activity in both groups basically corresponded to low-I (75% and 38%) and medium-II (16.7% and 38%) degrees of activity.

According to the stage of X-ray changes in the joints, the ratio of sick children was almost the same and was expressed in the prevalence of stages I (41.7% and 51.7%) and II (33.3% and 34.5%). Only 1 patient (8.3%) with a positive level of anti-CCP and anti-MCV had stage IV radiological changes with the formation of fibrous ankylosis.

Functional disorders of the joints in the group of patients seropositive for antibodies to citrullinated peptides were of a similar nature compared to the group of seronegative patients and in most cases were within the first 2 degrees (I degree - 16.7% and 13.8%, II degree - 58.3% and 82.8% respectively).

Conclusion

Thus, in patients seropositive for antibodies to citrullinated peptides, polyarthritis was formed in more than 70% at the time of examination, regardless of the type of disease onset. However, comparing the clinical characteristics of the articular syndrome (disease activity, functional disorders of the joints, X-ray stage, damage to small joints of the hands, etc.) in the groups of seropositive and seronegative for anti-citrullinated antibodies of patients with JIA with polyarthritis, we did not find significant differences. It should only be noted that in all 12 seropositive patients the detected polyarthritis was symmetrical in 100% of cases, which is significantly more frequent ($p < 0.01$) than in seronegative patients (16 out of 29).

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