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Subclinical Inflammation as A Factor of Early Cardiovascular Risk in Children with Juvenile Arthritis

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Abstract: Subclinical inflammation in juvenile idiopathic arthritis (JIA) is considered a key mechanism in the development of early cardiovascular disorders that remain undiagnosed for a long time.

Objective. To evaluate the role of subclinical inflammation in the development of early cardiovascular changes in children with JIA.

A total of 80 children with JIA were examined: 50 with the systemic variant and 30 without systemic manifestations. Clinical and instrumental studies (ECG, Holter monitoring, echocardiography) were performed, along with determination of IL-6, TNF-α, VEGF, IL-8, and NT-proBNP levels.

Results. Elevated levels of proinflammatory cytokines were found to be associated with subclinical myocardial remodeling, conduction abnormalities, and valvular dysfunction. Significant correlations were identified between IL-6, TNF-α, IL-8, and indices of left ventricular hypertrophy and dilation (r=0.53–0.75; p<0.05–0.01). Increased VEGF reflected activation of angiogenesis and was associated with myocardial structural changes, while NT-proBNP was related to functional dysfunction.

Conclusion. Subclinical inflammation is an important factor in the development of early cardiovascular risk in children with JIA and may serve as a basis for developing prognostic models.

Keywords: Juvenile idiopathic arthritis, children, subclinical inflammation, IL-6, TNF-α, VEGF, cardiovascular risk.

Introduction: Juvenile idiopathic arthritis is a chronic inflammatory disease in which immune mechanisms lead not only to joint damage but also to systemic changes, including involvement of the cardiovascular system.

In recent years, increasing attention has been paid to the role of subclinical inflammation as a determinant of early stages of the cardiovascular continuum. Even in the absence of pronounced clinical symptoms, persistent cytokine activation may lead to structural and functional myocardial changes.

Studying the relationship between immunoinflammatory markers and cardiovascular parameters is important for early diagnosis and prevention of complications.

METHODS

The study included 80 children with JIA. The main group consisted of 50 patients with the systemic variant, and the comparison group included 30 children without systemic manifestations.

The mean age was 10.8 ± 0.6 years.

The following were performed: echocardiography (EDV, LV dimensions, ejection fraction, interventricular septum thickness), electrocardiography and Holter monitoring, and measurement of IL-6, TNF-α, VEGF, IL-8, and NT-proBNP levels.

Statistical analysis included correlation analysis and assessment of significance ($p < 0.05$).

RESULTS

The study demonstrated that children with JIA, even in the absence of pronounced clinical symptoms, develop a complex of subclinical cardiovascular changes closely associated with immune-inflammatory activity. These abnormalities were most pronounced in patients with

the systemic variant, highlighting the importance of generalized inflammation in cardiac involvement.

Echocardiographic analysis revealed a tendency toward increased end-diastolic volume and left ventricular size, as well as thickening of the interventricular septum, reflecting myocardial dilation and hypertrophy. These changes were predominantly subclinical and not accompanied by significant complaints, but their frequency increased with disease activity.

Rhythm and conduction disturbances were mainly observed in patients with high inflammatory activity and included sinus tachycardia, supraventricular extrasystoles, and intraventricular conduction abnormalities, indicating involvement of the cardiac conduction system.

Valvular dysfunction manifested as grade I–II mitral and tricuspid regurgitation and tended to progress with longer disease duration, suggesting a role of chronic inflammation and myocardial remodeling. Left ventricular dilation was detected in 30.0% of children in the main group versus 6.6% in the comparison group ($p<0.01$). Reduced ejection fraction was observed in 12.0% and 3.3%, respectively ($p<0.05$). Rhythm and conduction disturbances were noted in 26.0% of patients in the main group and 10.0% in the comparison group ($p<0.05$). Mitral regurgitation occurred in 34.0% vs 13.3% ($p<0.05$), and tricuspid regurgitation in 28.0% vs 10.0% ($p<0.05$) (tab.1).

Table 1.

Cardiovascular abnormalities in children with juvenile idiopathic arthritis (%)

Parameter	Systemic variant (n=50)	Without systemic manifestations (n=30)	p-value
Left ventricular dilation	30.0	6.6	<0.01
Rhythm disturbances	26.0	10.0	<0.05
Mitral regurgitation	34.0	13.3	<0.05
Tricuspid regurgitation	28.0	10.0	<0.05
Reduced ejection fraction	12.0	3.3	<0.05

Analysis of immunoinflammatory markers showed significantly higher levels of IL-6, TNF-α, and IL-8 in the systemic group. Significant correlations were found between disease activity and left ventricular hypertrophy ($r =0.75$; $p<0.01$), as well as conduction disturbances ($r=0.53$; $p<0.05$). Disease duration correlated with the severity of mitral ($r=0.65$; $p<0.01$) and tricuspid regurgitation ($r=0.72$; $p<0.01$).

Elevated IL-6, TNF-α, and IL-8 levels were associated with myocardial structural changes, including dilation and hypertrophy ($r=0.53–0.75$; $p<0.05–0.01$), indicating a direct role of subclinical inflammation in remodeling processes.

VEGF levels were significantly higher in the main group ($p<0.01$) and correlated with interventricular septum thickness ($r=0.58$; $p<0.01$), reflecting angiogenesis activation. NT-proBNP levels were also higher and negatively correlated with ejection fraction ($r =–0.62$; $p<0.01$), indicating early myocardial dysfunction.

These findings suggest that even subclinical inflammatory activation directly affects the morphofunctional state of the heart.

Increased VEGF was associated with more pronounced myocardial changes and correlated with septal thickness and valvular regurgitation severity, reflecting angiogenesis and vascular remodeling. Chronic inflammation and excessive VEGF production may lead to abnormal vascular network formation, impaired microcirculation, and progression of myocardial remodeling.

NT-proBNP concentration increased in patients with more significant echocardiographic changes and was associated with myocardial functional status, including reduced contractility, confirming its role as an early marker of myocardial stress.

The identified relationship between immunoinflammatory markers and cardiovascular changes suggests that subclinical inflammation acts as an integrative pathogenic factor. Persistent cytokine activation contributes to endothelial dysfunction, impaired vascular tone regulation, angiogenesis activation, and myocardial remodeling, forming the basis for clinically significant cardiovascular complications.

CONCLUSION

Subclinical inflammation in children with juvenile idiopathic arthritis is a leading factor in the development of early cardiovascular changes. Elevated levels of proinflammatory cytokines and angiogenic factors are associated with myocardial remodeling and functional cardiac impairment, supporting the need for early cardiological monitoring and risk stratification.

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