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MYOCARDITIS IN CHILDREN (LITERATURE REVIEW)

Shakhzoda Rustamovna Odilova

1st year master's resident of the Department of Pediatrics and Neonatology of Samarkand State Medical University

SAMARKAND, UZBEKISTAN

Maksim Vyacheslavovich Lim

DSc., Associate Professor of the Department of Pediatrics and Neonatology of Samarkand State Medical University

SAMARKAND, UZBEKISTAN

Introduction

Myocarditis in children is an inflammatory disease of the heart muscle (myocardium) that occurs in most cases as a result of infectious damage or an autoimmune process [1,2]. According to the World Health Organization (WHO), myocarditis remains one of the important causes of hospitalizations in pediatric practice, especially in preschool and early school-age children [3]. Meanwhile, the true prevalence of childhood myocarditis may be underestimated due to diagnostic difficulties and frequent asymptomatic or mildly symptomatic course [4].

In modern pediatrics, there is a wide range of diseases capable of causing inflammatory damage to the myocardium. Etiological factors can be viruses (enteroviruses, parvovirus B19, influenza virus, SARS-CoV-2, etc.), bacteria (streptococci, staphylococci, mycoplasmas), as well as parasitic and fungal agents [5]. Viral etiology leads among the causative agents of myocarditis in children, as reported by both Russian and foreign researchers [6]. Additionally, the autoimmune component plays an important role in the pathogenesis of myocarditis: when an infectious agent enters a child's body, the immune system is activated, which can lead to damage of cardiomyocytes by their own antibodies [7].

The diagnosis of myocarditis in children traditionally includes a complex of clinical, laboratory, and instrumental methods. Along with general assessment of the child's condition, the doctor pays attention to the presence of intoxication symptoms, arrhythmias, changes on electrocardiogram (ECG), signs of inflammation according to laboratory tests (increased troponin levels, inflammation markers, creatine kinase-MB) [10]. Echocardiography (EchoCG) is highly informative, allowing detection of myocardial contractility disorders, heart chamber dilation [11]. Cardiac magnetic resonance imaging (MRI) with contrast is increasingly used in pediatric practice, providing detailed visualization of inflammatory changes and myocardial fibrosis [12].

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Regarding treatment, it primarily aims at combating the etiological factor and reducing the inflammatory reaction in the heart muscle. Antiviral, antibacterial, or antifungal drugs are used (depending on the pathogen), immunotropic therapy (immunoglobulins, corticosteroids), as well as supportive therapy (ACE inhibitors, beta-blockers, diuretics in case of heart failure development) [13]. Timely and adequate therapy can prevent the development of severe complications, including dilated cardiomyopathy, which can be an outcome of recurrent or chronic myocarditis [14].

However, despite advances in diagnosis and treatment, myocarditis in children remains difficult for timely detection and differential diagnosis with other cardiovascular system pathologies (for example, rheumatic heart disease, congenital heart defects, cardiomyopathies) [15]. The key importance lies in the search and verification of the infectious agent, as well as the assessment of autoimmune mechanisms forming persistent inflammation [16].

The scientific literature emphasizes the role of early diagnosis of childhood myocarditis, since it is in the early stages that severe initial damage to the heart muscle can be prevented [17]. Modern research actively studies genetic and epigenetic aspects determining the child's response to the introduction of pathogenic agents [18]. An important direction is the improvement of laboratory testing methods, particularly the introduction of highly sensitive biomarkers of myocardial damage (high-sensitivity troponin, galectin-3, etc.) [19].

The purpose of this literature review is to systematize modern data on the etiology, pathogenesis, diagnosis, and treatment of myocarditis in children, as well as to analyze factors affecting the disease prognosis. The article presents information from domestic and foreign sources with an emphasis on the latest achievements in the field of pediatric cardiology and infectious diseases [20].

Below is a detailed analysis of scientific literature devoted to various aspects of myocarditis in children, including epidemiology, main etiological factors, pathogenetic mechanisms, clinical manifestations, diagnostic methods, therapeutic approaches, and prognosis.

Epidemiology of Myocarditis in Children

Current epidemiological data indicate that the frequency of myocarditis among children can range from 1 to 10 cases per 100,000 pediatric population, depending on the geographic region and applied diagnostic criteria [1,2,4]. The variation in indicators is associated with both statistical accounting peculiarities and differences in the availability of modern diagnostic methods.

According to Russian studies, the proportion of myocarditis among all circulatory system diseases in children ranges from 5-7% [5,16]. It is noted that during outbreaks of viral infections (especially enterovirus or influenza nature), the number of detected myocarditis cases increases [2,6]. This is explained by the leading role of viral etiology, where viruses directly damage cardiomyocytes or trigger autoimmune mechanisms of inflammation [7].

The most vulnerable age group is considered to be preschool children, which is associated with the imperfection of their immune system and higher susceptibility to infectious agents

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[8]. It is also noted that in adolescents, myocarditis may develop against the background of severe viral infection courses, bacterial complications, or in the presence of predisposing factors (hypovitaminosis, chronic infection foci) [9].

Etiological Factors

The main causative agents of myocarditis in children are viruses of the picornavirus family (Coxsackie B enteroviruses, ECHO), parvovirus B19, herpesviruses (including Epstein-Barr virus), influenza virus, respiratory syncytial virus, adenovirus, as well as SARS-CoV-2 [5,6,21]. Bacterial etiology is more often associated with diphtheria (Corynebacterium diphtheriae), streptococcal and staphylococcal infections [22]. Opportunistic microorganisms (mycoplasmas, chlamydiae) and fungi (Candida spp.) usually cause myocarditis in weakened children with comorbidities or immunodeficiencies [23].

Some parasitic diseases (Chagas disease, toxoplasmosis) in rare cases can lead to specific myocarditis [24]. Autoimmune processes (systemic lupus erythematosus, juvenile rheumatoid arthritis) can also cause inflammatory heart damage, although usually accompanied by polysyndromic manifestations [25].

Pathogenesis

The pathogenesis of myocarditis in children consists of the direct cytopathic effect of the pathogen on cardiomyocytes and immune system activation [7]. In the early stages, the virus penetrates myocardial cells using specific receptors (e.g., Coxsackie-adenovirus receptor - CAR), leading to cardiomyocyte necrosis and release of intracellular antigens [6].

Subsequently, innate and adaptive immunity is activated, increasing production of pro-inflammatory cytokines (interleukin-1, interleukin-6, tumor necrosis factor-α, etc.), which in turn attracts leukocytes, macrophages, and T-lymphocytes to the inflammation zone [7,26]. Gradually, a myocardial inflammatory infiltrate forms. At the stage of autoimmune response, antibodies to cardiomyocyte structures form, intensifying damage to heart tissue elements [25,27].

As a result of prolonged inflammatory process, significant numbers of cardiomyocytes may die and be replaced by connective tissue fibers, leading to heart chamber dilation, decreased contractile function, and progression of heart failure (formation of so-called inflammatory dilated cardiomyopathy) [28].

Classification and Clinical Forms

In clinical practice, classification based on the duration of myocarditis course is often used:

1. Acute myocarditis: up to 1-2 months from disease onset.

2. Subacute myocarditis: 2-6 months.

3. Chronic myocarditis: over 6 months, with possible periodic relapses [8,29].

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By severity of course, mild, moderate, and severe forms are distinguished, differentiated based on the severity of heart failure symptoms, contractile function indicators (ejection fraction), and presence of arrhythmias [10,11]. Also identified are oligosymptomatic variants of myocarditis, which are often diagnosed post-factum, during routine examinations or after respiratory infections [1,17].

In young children, myocarditis may present with predominance of general intoxication symptoms, respiratory disorders, refusal to eat, restlessness or lethargy, sometimes complicating early diagnosis [30].

Clinical Picture

Clinical manifestations of childhood myocarditis may be nonspecific, especially in the early stages. The most typical symptoms include [1,9,22]:

- General weakness, increased fatigue, reduced appetite;

- Tachycardia or, less frequently, bradycardia;

- Shortness of breath (especially in infants) during feeding, crying, physical activity;

- Complaints of chest pain or behind the sternum in older children;

- Heart rhythm disturbances (extrasystole, paroxysmal tachycardia, etc.);

- Possible liver enlargement, edema (with right ventricular failure).

In severe cases, cardiogenic shock or acute heart failure develops in the child with pronounced hypotension and organ perfusion disorders [26,31]. In some cases, myocarditis may manifest suddenly, in the form of acute decompensation, requiring emergency hospitalization.

Clinical and Laboratory Diagnosis

Diagnosis of myocarditis in children is based on a combination of clinical signs, physical examination data (heart auscultation, measurement of heart rate, blood pressure), and laboratory tests [10]. Complete blood count reveals signs of inflammation (leukocytosis, elevated ESR), biochemical blood analysis may show increased markers of myocardial damage (troponin I or T, creatine kinase-MB) [11].

Levels of C-reactive protein (CRP), procalcitonin, cytokines (IL-6, TNF-α) are also assessed, allowing judgment of the degree of inflammatory process [28]. Virological and serological studies (antibody determination, PCR diagnostics) help identify the causative agent of myocarditis [6,32].

Instrumental Methods

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- Electrocardiography (ECG): can detect signs of rhythm disturbances (extrasystole, conduction blocks) and ST segment, T wave changes characteristic of inflammatory process in the myocardium [10].

- Echocardiography (EchoCG): the main visualization method for assessing contractile function, heart wall thickness, chamber sizes, presence of pericardial effusion [11].

- Holter ECG monitoring: allows more detailed assessment of arrhythmia episodes throughout the day [33].

- Cardiac MRI: with gadolinium contrast provides ability to identify areas of myocardial inflammation and fibrosis, clarify diagnosis and extent of damage [12,34].

- Endomyocardial biopsy: indicated in complex cases when morphological confirmation of diagnosis and determination of inflammatory process activity is necessary. Dallas criteria are used, describing histological manifestations of myocarditis (presence of inflammatory infiltrate and cardiomyocyte necrosis) [31,35].

General Principles and Etiotropic Therapy

Treatment of myocarditis in children includes several directions: combating the causative agent (etiotropic therapy), reducing inflammatory process activity, and supporting heart function [13]. With confirmed viral etiology, antiviral agents (interferons, ribavirin) may be used, though their effectiveness in the pediatric population requires further research [5,36].

For bacterial myocarditis, antibiotics corresponding to the pathogen's sensitivity spectrum (penicillins, cephalosporins, etc.) are prescribed; for diphtheritic myocarditis - antidiphtheritic serum and antibiotics [22]. In case of detected fungal or parasitic infection, appropriate antifungal and antiparasitic drugs are used [23,24].

Immunotropic and Pathogenetic Therapy

In severe cases of myocarditis, with autoimmune signs or pronounced inflammatory activity, glucocorticosteroids (prednisone, methylprednisolone) may be prescribed [7,25]. In some cases, intravenous administration of immunoglobulin has a positive effect, helping neutralize circulating autoantibodies and reduce inflammation [13,37].

The use of immunosuppression remains debatable and is conducted under strict control, as suppression of the immune system during active viral replication may exacerbate the infectious process [38].

Supportive and Symptomatic Therapy

To support heart contractile function, inotropic agents (dobutamine, dopamine) are used in intensive care conditions for severe cases [31]. Diuretics (furosemide, spironolactone) are prescribed for signs of congestion in the large or small circulation [39]. ACE inhibitors (enalapril, captopril) and beta-blockers (metoprolol, bisoprolol) help reduce afterload and improve heart remodeling in case of chronic heart failure development [13,32].

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Special importance is placed on regimen: the child should maintain relative rest, avoiding intense physical activity until complete recovery or stabilization of heart function indicators [9].

Prognosis and Complications

The prognosis for myocarditis in children depends on etiology, severity degree, timeliness of diagnosis, and initiated therapy. Overall, in mild and moderate forms, especially of viral origin, with adequate treatment, complete regression of changes and restoration of contractile function is possible [1,37].

However, in severe myocarditis accompanied by heart failure and arrhythmias, the risk of complications significantly increases. Among the most dangerous consequences are [9,13,31]:

- Dilated cardiomyopathy;

- Chronic heart failure;

- Rhythm disturbances (ventricular tachycardias, complete heart blocks);

- Thromboembolic complications (with pronounced chamber dilation);

- Cardiogenic shock and fatal outcome in the acute period.

With adherence to rehabilitation principles and regular dynamic monitoring, a significant portion of children can avoid severe complications and maintain satisfactory or nearly normal heart function [40].

Prevention

There is no specific prevention for myocarditis, but it is important to take measures to reduce infection risks and timely treat chronic inflammation foci. In particular [16,25]:

- Conducting vaccinations against influenza and other respiratory infections;

- Observing sanitary-hygienic standards in children's groups;

- Timely treatment of acute respiratory and bacterial diseases (especially sore throat, sinusitis, pneumonia);

- Monitoring chronic infection foci (caries, tonsillitis, etc.);

- Using personal protective equipment (masks, antiseptics) during epidemics;

- Healthy lifestyle, balanced nutrition, and adequate physical activity.

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Early diagnosis of myocarditis in children, especially with symptoms indicating heart pathology after an infection, is crucial in preventing disease progression [17,35].

Discussion

Analysis of modern research shows that myocarditis in children should be considered a multifactorial disease, based on both infectious and autoimmune mechanisms [1,7]. Viral agents play a leading role in initiating the inflammatory cascade, however, subsequent autoimmune reorganization may sustain the pathological process even after pathogen elimination [6,25].

Improvement of laboratory methods (PCR, high-sensitivity biomarkers, serology) and visualization technologies (contrast-enhanced cardiac MRI) expands possibilities for early diagnosis and allows individualization of therapeutic tactics [12,34,36]. However, questions of differential diagnosis between myocarditis and some forms of idiopathic dilated cardiomyopathy remain unresolved, especially when there are no obvious signs of infectious process [28].

The literature emphasizes the need for an interdisciplinary approach: involvement of pediatrician, cardiologist, infectious disease specialist, rheumatologist, and immunologist for comprehensive patient assessment [16,22]. Close collaboration of specialists helps timely identify secondary autoimmune reactions, select optimal immunotherapy regimens, and assess the need for antiviral treatment [13,38].

An important aspect is the problem of residual myocardial changes and risk of developing dilated cardiomyopathy in the long term. According to some foreign sources, up to 30% of children who have experienced clinically expressed myocarditis may show signs of chronic heart failure within 5-10 years [7,31]. Therefore, monitoring cardiovascular system status during remission, active rehabilitation, and prevention of repeated infection episodes become crucial [39,40].

Conclusion

1. Myocarditis in children is a multifactorial inflammatory lesion of the heart muscle, most often caused by viral agents.

2. Etiological factors include enteroviruses, parvovirus B19, adenoviruses, influenza viruses, bacteria (diphtheria, streptococci), etc.; pathogenesis is based on direct cytopathic and autoimmune effects on cardiomyocytes.

3. Clinical manifestations vary from oligosymptomatic forms to severe conditions with heart failure and arrhythmias; non-specific symptoms (shortness of breath, lethargy, feeding refusal) are often observed in young children.

4. Diagnosis is based on combination of clinical picture, laboratory data (troponins, inflammation markers), visualization methods (EchoCG, cardiac MRI), electrocardiography; endomyocardial biopsy is performed if necessary.

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5. Treatment includes etiotropic (antiviral or antibacterial) therapy, immunotherapy (corticosteroids, immunoglobulins), and supportive heart failure therapy (ACE inhibitors, beta-blockers, diuretics).

6. Prognosis depends on timeliness of diagnosis and adequacy of treatment; some children fully recover, others may progress to chronic form with risk of developing dilated cardiomyopathy.

7. Prevention is based on reducing infection spread (vaccination, sanitation of chronic infection foci), healthy lifestyle, and increased physician vigilance regarding myocarditis, especially after viral diseases.

Thus, for improving outcomes of myocarditis in childhood, a comprehensive approach is necessary, including early detection, personalized therapy, strict disease course monitoring, and adequate rehabilitation. Further research should focus on improving objective diagnostic methods, clarifying pathogenetic mechanisms, and developing new therapeutic strategies considering genetic and immunological characteristics of a child's organism.

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