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Modern Approaches to Rheumatic Carditis in Children

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Annotation: In modern rheumatology, the timely and accurate diagnosis of acute rheumatic fever (ARF) remains a significant issue. The variety of forms and courses (clinical polymorphism), the blurring of clinical and laboratory symptoms, and the lack of specific tests for ARF often serve as sources of both underdiagnosis and overdiagnosis in clinical practice. The relevance of this issue is also linked to the identification of new nosological forms that share similar clinical symptoms with ARF but require fundamentally different therapeutic approaches.

Keywords: mitral valve lesions, rheumatic heart disease, mitral stenosis, mitral regurgitation.

Rheumatic carditis is the leading syndrome of acute rheumatic fever (ARF), associated with the majority of diagnostic challenges and errors. A fundamental component of carditis is valvulitis (primarily of the mitral valve, less commonly of the aortic valve), which may be accompanied by myocarditis or myopericarditis (pancarditis). Upon auscultation, these patients exhibit an organic heart murmur. Three main types are identified: a) a blowing systolic murmur at the apex of the heart associated with the first heart sound (caused by mitral regurgitation); b) a transient low-frequency mesodiastolic murmur in the mitral area; and c) a high-frequency decreasing protodiastolic murmur heard along the left sternal border (associated with aortic regurgitation).

Heart damage in the form of myocarditis or myopericarditis, without valvulitis, is universally considered unlikely in ARF and warrants a thorough differential diagnosis with carditis of other etiologies (see further).

In the presence of pronounced arthritis or mild chorea, the clinical symptoms of carditis in ARF may be weak. As a result, the diagnostic significance of echocardiography (ECHO) with Doppler technology increases, as it allows for the evaluation of the anatomical structure of the heart and the status of intracardiac blood flow, including the identification of mitral or aortic regurgitation as an early sign of valvulitis.

Considering the above, ECHO data have been included in the "minor" modified diagnostic criteria for ARF.

On the other hand, due to the high sensitivity of ECHO, it is now possible to detect afonic, i.e., asymptomatic, valvular regurgitation (VR). This phenomenon often causes difficulties in proper interpretation because it can be found in healthy individuals. According to the American Heart Association, the presence of mitral and, less frequently, aortic afonic VR is not a sufficient basis for the diagnosis of rheumatic valvulitis. However, according to domestic authors, when differentiating minimal VR in individuals with structurally normal hearts, it is essential to consider not the hemodynamic characteristics of the regurgitation itself, but the condition of the mitral valve leaflets, which should be carefully assessed using quantitative parameters – the thickness index and the extent of thickening of the anterior mitral leaflet.

A conclusion of "physiological" regurgitation can only be made after comprehensive electrocardiographic (ECG) testing, including Holter monitoring, determining laboratory parameters of ARF, and conducting a follow-up ECHO after several weeks.

An important feature of carditis during the first attack of acute rheumatic fever (ARF) is the clear positive dynamics under the influence of active anti-rheumatic therapy. In the vast majority of cases, treatment leads to normalization of heart rate, restoration of tone clarity, reduction in the intensity of systolic and diastolic murmurs, reduction in the heart's size, disappearance of circulatory insufficiency symptoms, and a decrease in laboratory parameters indicating disease activity.

Rheumatic carditis has the following characteristics:

Chronological association with throat infections (pharyngitis, tonsillitis) caused by Group A beta-hemolytic streptococcus (GABHS). Latent period of 2–4 weeks. Young age of the patient. Predominantly acute or subacute onset. Polyarthritis or acute arthralgia at the onset of the disease. "Passive" nature of cardiac complaints. Presence of valvulitis. High mobility of carditis symptoms. Correlation between laboratory and clinical signs of disease activity.The list of nosological forms included in the differential diagnosis algorithm for rheumatic carditis is broad: Infective endocarditis (IE), Non-rheumatic myocarditis, Neurocirculatory dystonia, Idiopathic mitral valve prolapse, Cardiomyopathies, Heart myxoma, Primary antiphospholipid syndrome, Nonspecific aortoarteritis, Kawasaki disease, Systemic lupus erythematosus (SLE), Ankylosing spondylitis, Reactive arthritis, Calcified (degenerative) aortic stenosis.

Among these diseases, the most concerning and requiring priority exclusion or confirmation is infective endocarditis. It can affect both unchanged heart valves—primary IE—and complicate an existing rheumatic heart disease (RHD) with secondary IE. The high mortality rate (up to 20%) in IE necessitates its prompt recognition and thorough differential diagnosis.

When collecting a medical history, it's important to determine whether the patient has undergone any medical procedures in the past 1–2 months that may have involved bacteremia (especially dental procedures), experienced purulent infections, or suffered infected injuries. The use of drugs, particularly intravenous drug use, should also be considered. It's important to note that in a significant number of IE patients, no clear bacteremia-inducing factor is identified, so its absence should not be a definitive reason to exclude the disease.

The earliest symptom of IE is a fever of an irregular type, accompanied by chills of varying severity, followed by profuse sweating. Unlike ARF, the fever in IE rarely fully resolves with the use of anti-inflammatory drugs alone. IE is characterized by progressive weakness, anorexia, and rapid weight loss (up to 10–15 kg). In primary IE, isolated damage to the aortic valve with rapid development of regurgitation is more common. In staphylococcal IE, signs of severe regurgitation (due to almost complete valve destruction) and severe heart failure may appear within 7–20 days.

In IE involving the mitral valve, unlike rheumatic mitral regurgitation, symptoms of congestive heart failure due to pulmonary circulation overload appear early, due to the severe destruction of valve structures, leading to overload of the left heart chambers.

Early and frequent manifestations of IE include thromboembolisms in various locations (kidneys, spleen, brain). Peripheral signs of IE (e.g., Lukin-Liebman sign, Osler's nodes, Janeway lesions) are now rare but remain highly specific to the disease and, therefore, are important in differential diagnosis. Specific changes in the nails (e.g., "drumstick" fingers and "watch glass" nails) typically appear in the late stages of the disease and indicate its advanced nature and poor prognosis.

Key laboratory findings in the differential diagnosis of ARF and IE include progressive anemia, a pronounced and persistent left shift in the leukocyte count, hypergammaglobulinemia, the appearance of rheumatoid factor, and a positive blood culture. It's important to note that microbiological blood tests can yield negative results due to prior antibiotic treatment (which reduces pathogen detection to 35–40%), improper blood sample collection or transportation, low-quality microbiological techniques, or the nature of the pathogen.

A significant aid is provided by echocardiographic (EchoCG) data, especially transesophageal echocardiography, which allows for the detection of vegetations on valves and chordae, perforations or ruptures of valve leaflets, chordal ruptures, myocardial abscesses, and assessment of the degree and dynamics of cardiac conditions.

In clinical practice, the correct interpretation of vegetations detected by EchoCG can be challenging, particularly those resulting from thrombotic nonbacterial endocarditis (NBTE) in febrile patients with tumors or localized infections (e.g., sinusitis or urinary tract infections). This situation occurs quite frequently. It is noteworthy that in NBTE, thrombotic deposits are typically located primarily on the valves of the left side of the heart, usually on the ventricular surface of the mitral valve, have a broad base, and are 2–4 mm in size.

In cases of late rheumatic carditis, when more than two months have passed from the onset of a streptococcal infection (GABHS) preceding the development of acute rheumatic fever (ARF) to the patient's examination and laboratory studies, the levels of antistreptococcal antibodies tend to decrease or may even be normal.

In such situations, distinguishing between carditis (valvulitis) in ARF and non-rheumatic myocarditis (mostly viral) poses challenges. Features typical of non-rheumatic myocarditis syndrome include:

A chronological association with acute nasopharyngeal (often viral) infection; Shortened (<5–7 days) or absent latent period; Gradual onset of the disease; Absence of arthritis and pronounced arthralgia; Clear clinical, ECG, and EchoCG signs of myocarditis; Absence of valvulitis; Symptoms of asthenia and thermoregulation disturbances; Discrepancy between clinical and laboratory parameters; Slow dynamics under anti-inflammatory therapy.

In recent years, rheumatologists have increasingly observed patients requiring differential diagnosis between neurocirculatory dystonia and recurrent attacks of ARF. The majority of this category comprises middle-aged individuals, often women, who were mistakenly diagnosed with ARF in childhood.

The most characteristic signs of neurocirculatory dystonia are: A history of autonomic-endocrine dysfunction; More frequent association with stress factors; Gradual onset; Astheno-neurotic type of cardiac complaints (e.g., sensations of "stopping" or "pausing" of the heart, "air hunger," dissatisfaction with breathing, etc.); Periodic autonomic-vascular crises; Absence of clinical symptoms of valvulitis, myocarditis, and pericarditis; Absence of laboratory markers of inflammatory activity.

- Lack of effect from antirheumatic therapy; Worsening of the condition during glucocorticoid treatment; Improvement with tranquilizers and β-blockers.

A pronounced discrepancy between the abundance of complaints and the scarcity of clinical symptoms is striking. During objective heart examinations in such patients, a functional systolic murmur is often detected (in approximately 70% of cases), along with pronounced pulse and blood pressure variability. On ECG, transient changes in the terminal portion of the ventricular complex, such as T-wave flattening or inversion, are often observed. These changes, in the absence of myocardial dystrophy, show positive dynamics with medication trials using potassium chloride or propranolol. Despite a "long rheumatic history" and "frequent recurrent rheumatic attacks," no valvular heart disease can be identified in these patients.

Neurotic symptoms are often noted in idiopathic mitral valve prolapse (MVP), especially in young women. Most patients have an asthenic body type and one or more phenotypic signs of congenital connective tissue dysplasia, such as pectus excavatum, scoliosis of the thoracic spine, joint hypermobility syndrome, early development of severe flatfoot, etc. These patients have no history of acute rheumatic fever (ARF). Heart pathology is often detected incidentally, frequently during routine check-ups.

The diagnosis is usually made based on characteristic auscultatory findings (a mid-systolic "click" and late systolic murmur in the mitral valve projection zone) and confirmed using EchoCG. It should be noted that in 7–10% of cases, MVP may develop after rheumatic carditis. Distinctive EchoCG features of rheumatic MVP include: a) Prolapse of the thickened edge of the anterior mitral leaflet while its body remains properly aligned with the fibrous ring; b) Post-inflammatory changes in the leaflet.

EchoCG also helps in differentiating rheumatic carditis from cardiomyopathies, primarily hypertrophic cardiomyopathy. Systemic inflammatory symptoms (fever, weakness, weight loss, anemia, elevated ESR, dysproteinemia, etc.), combined with the auscultatory findings of mitral valve disease, require differentiation between recurrent ARF attacks and left atrial myxoma. Clinical signs suggesting myxoma include shorter disease duration, episodes of thromboembolism while maintaining sinus rhythm, and symptom severity depending on body position. The auscultatory pattern may resemble that of mitral stenosis. During systole, the myxoma is forcefully ejected from the left ventricle through the atrioventricular opening into the left atrium, delaying mitral valve closure and causing a split first heart sound with accentuation of its second component. The second heart sound is accentuated due to increased pulmonary artery pressure.

During diastole, an additional sound can be heard, produced by the tumor's abrupt cessation of motion as it strikes the endocardium of the left ventricle or as blood flow abruptly stops its movement. This "tumor plop" may resemble the opening snap of the mitral valve. Most patients also have mid-diastolic and systolic murmurs at the heart apex. A distinctive feature of heart sounds in left atrial myxoma, as with other localizations, is the variability in murmur and tone intensity depending on body position and over time. The murmur of mitral regurgitation can be loud and pansystolic, often associated with significant damage to the valve leaflets or chordae caused by the calcified tumor's constant motion.

The diagnosis is typically made via transthoracic EchoCG, which provides clear visualization of the shape, size, and attachment of the tumor in the left atrium. Transesophageal EchoCG and MRI are rarely required for diagnostic clarification.

When evaluating a patient with isolated carditis (valvulitis) in ARF, it is often necessary to differentiate it from heart involvement within the framework of antiphospholipid syndrome (APS). APS is a unique syndrome characterized by arterial and/or venous thrombosis in any location, neurological symptoms (e.g., chorea, seizures, cerebral ischemia), cardiac issues (valve disease, myocardial infarction), skin symptoms (livedo reticularis, leg ulcers), renal symptoms (renal failure, nephrogenic hypertension), hematological disorders (hemolytic anemia), thrombocytopenia, and the presence of lupus anticoagulant, antiphospholipid antibodies (aPL), cardiolipin antibodies, and β2-glycoprotein antibodies.

According to the 2006 international consensus recommendations, the diagnosis of aPL-associated valvular heart disease requires:

Presence of aPL (meeting laboratory criteria for APS) plus EchoCG findings of valvular pathology, regurgitation, and/or stenosis of the mitral or aortic valve, or any combination thereof; Use of transthoracic ± transesophageal EchoCG; Valvular pathology criteria, including: Thickening of the valve leaflets >3 mm; Local thickening involving the proximal or mid-portion of the leaflet; Irregular nodules on the atrial surface of the mitral valve and/or the vascular surface of the aortic valve. The presence and severity of regurgitation and/or stenosis should be assessed via Doppler EchoCG. Interpretation of results should involve consultation with two EchoCG specialists.

Functional capacity and cardiac status should be assessed according to the revised criteria of the New York Heart Association for diagnosing heart diseases.

In all the cases mentioned above, acute or previous rheumatic fever (ARF) and infective endocarditis (IE) must be ruled out.

Patients meeting the clinical criteria for antiphospholipid syndrome (APS) should not be evaluated using this scale.

Diagnosis of systemic lupus erythematosus (SLE) should adhere to the criteria established by the American College of Rheumatology (ACR).

Differentiation of Carditis in ARF and Takayasu Arteritis

For Takayasu arteritis, particular attention should be paid to transient paresthesia, intermittent claudication, asymmetry or absence of pulses in the radial, ulnar, or carotid arteries, differences in blood pressure between limbs, and pathological vascular murmurs auscultated over carotid, subclavian, femoral arteries, and along the aorta.

The diagnosis is confirmed via duplex scanning of neck vessels, CT, or MRI angiography. The current diagnostic criteria for Takayasu arteritis (adopted by ACR) include evidence from contrast angiography, such as narrowing or occlusion of the aorta and its major branches (proximal segments of the upper and lower limbs), not associated with atherosclerosis, fibromuscular dysplasia, or similar conditions (focal or segmental changes).

Kawasaki Disease

Challenges in distinguishing ARF from Kawasaki disease may arise, especially in individuals of Mongoloid descent. Kawasaki disease, often accompanied by valvulitis and valve insufficiency, is characterized by the following:

Antibiotic-resistant fever lasting 5 or more days.

Bilateral conjunctivitis.

Typical changes in the lips and oral cavity (hyperemia, swelling, dryness of the lips, "strawberry" tongue, diffuse mucosal involvement in the mouth and pharynx).

Acute, non-purulent cervical lymphadenopathy.

Polymorphic rash, primarily on the torso.

Changes in the hands and feet (erythema of palms and soles, swelling during the acute phase, and skin peeling during recovery).

A Kawasaki disease diagnosis is valid with five out of six symptoms or a combination of four symptoms plus coronary artery aneurysms confirmed by two-dimensional EchoCG or coronary angiography.

Systemic Lupus Erythematosus (SLE)

The diagnosis of SLE is strongly associated with female gender, hair loss, erythema on the cheeks and over the zygomatic arches, photosensitivity, and oral or nasal ulcers. Pericarditis is the most common cardiac symptom, while Libman–Sacks endocarditis develops later and signifies high disease activity with pronounced polysyndromic manifestations.

It is important to note that antinuclear antibodies (ANA) and anti-native DNA antibodies may also be present in infective endocarditis, but repeated detection at high titers is more characteristic of SLE.

Ankylosing Spondylitis

Heart involvement in ankylosing spondylitis may manifest as aortitis with aortic and mild mitral regurgitation. More commonly, asymptomatic EchoCG changes such as a ridge at the base of the anterior mitral leaflet, root dilation, thickening of the aorta, and thickening of the aortic valve leaflets are observed.

Aortic Stenosis and Reactive Arthritis

Calcific aortic stenosis is characterized by:

A harsh systolic murmur over the aorta, radiating to the neck vessels.

Age over 60 years.

Absence of a rheumatic history.

Combination of clinical symptoms: chest pain, dyspnea, syncope with exertion (Roberts' triad), palpitations, irregular heartbeats.

Embolic complications such as myocardial infarction, stroke, pulmonary artery teleangiectasia, sudden vision loss, or limb arterial thrombosis.

Gastrointestinal bleeding after age 65, unrelated to peptic ulcers.

First appearance of a heart murmur after age 55.

Nodular Erythema

Nodular erythema, often developing after streptococcal infections with joint involvement, is not associated with valvulitis or worsening valvular pathology, even in patients with a confirmed rheumatic history. Nodular erythema does not reflect rheumatic activity and is not characteristic of ARF itself.

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