Cardiac function in juvenile rheumatoid arthritis

Cardiac dysfunction is seen with many of the collagen vascular diseases including systemic lupus erythematosus, rheumatoid arthritis (RA), dermatomyositis, and systemic sclerosis. Juvenile rheumatoid arthritis (JRA) is the most common rheumatic disease in childhood with a very variable course. The second major cause of mortality in this disease is from cardiac involvement. This occurs in about 4.5% cases and includes pericarditis, aortitis, coronary vasculitis, valvulitis (endocarditis), conduction system involvement, pulmonary hypertension and myocarditis.

Proinflammatory cytokines, in particular tumor necrosis factor (TNF-α) and interleukin 6 (IL-6) play an important role in this disease and may be responsible for the damage seen with arthritis, rash, fever and serositis. Therapy includes pain management and reduction of the inflammatory process. Non steroidal anti-inflammatory drugs (NSAID) including COX-1 and COX-2 inhibitors, corticosteroids, methotrexate, sulfasalazine and other disease-modifying anti-rheumatic drugs are used with varying success. Newer anti-cytokine agents such as leflunomide and etanercept have been found to be effective in reducing disease progression in adult rheumatoid arthritis.

In most cases of RA, the cardiac disease is subclinical with early diastolic dysfunction followed by insidious onset of symptoms with increasing systolic dysfunction and cardiac failure which is a late finding. Abnormal diastolic function of the left ventricle has been reported in adult RA and JRA. In this issue of the Journal, Bharti et al studied systolic and diastolic function of the left ventricle in 35 patients and compared the data with age and sex matched controls. They demonstrate a higher blood pressure, higher heart rate, larger left ventricular dimension, lower left ventricular systolic function, and decreased diastolic function in JRA patients, compared to control population. The study did not find any differences in the left ventricular wall thickness or pericardial involvement. They conclude that there are significant systolic and diastolic functional abnormalities in asymptomatic juvenile rheumatoid arthritis patients and suggest monitoring the patients. The manuscript is reasonably well-written and has some merits, particularly documentation of left ventricular diastolic function abnormalities. But, there are several limitations in the study: The age range of study subjects is 7 to 28 years, and as such, many subjects are not truly children. Blood pressures are said to be higher, but indeed they are within normal range. Furthermore, all patients are receiving NSAID which may account for hypertension. The report also does not mention drugs other than NSAIDs taken by the study population. At the time of the study a sedimentation rate or C-reactive protein level may reflect the inflammatory status of the disease although many studies in adults have failed to correlate the degree of inflammation with the amount of diastolic or systolic dysfunction in RA. Large left ventricular size and volume may be related to lower hemoglobin levels. Ejection fraction and fractional shortening are indeed within normal range of established values; should they be called abnormal? The effect of increasing size of the child with time should be accounted for before concluding that increase in LV dimension is the effect of the disease. Despite all these limitations, we believe that this study supplements the limited literature available on cardiac involvement in JRA.

Increasing diastolic dysfunction has been found with increased duration of the disease but the etiology of this diastolic dysfunction is still unclear. The abnormal relaxation of the myocardium may be due to thickened and stiff pericardium, left ventricular hypertrophy, interstitial fibrosis, ischemic changes (resulting in abnormal relaxation of the ventricle) and/or amyloid infiltration. Thus, the cause of abnormal diastolic parameters may be multiple and may be a cumulative effect of several factors such as pericarditis with or without pericardial effusion, hypertension, left ventricular hypertrophy, therapy with cardiotoxic agents such as cyclosporine, gold salts, d-penicillamine, chlo-roquine, hydrochloroquine, hypertension due to steroid therapy, secondary amyloidosis, and vascular stiffness from vasculitis. The abnormal echocardiographic diastolic parameters may not be so much reflective of “myocarditis” because such myocarditis in JRA is a rare phenomenon and seen in only 1 to 10% cases, especially when there is severe active systemic disease. However, pericardial involvement can be seen in almost 45% of the cases at autopsy and collagen fiber involvement with endocarditis and pericarditis is more prevalent.

In conclusion, children with JRA are at risk for cardiac dysfunction. Routine cardiac evaluation, possibly yearly may be one way to monitor these children, as implied by the authors. Blood pressure measurement, electrocardiogram and echocardiogram may be performed. On an echocardiogram, evaluation of left ventricular wall thickness, pulmonary artery pressure, pericardial effusion, pericardial thickening, left ventricular diastolic and systolic function, left ventricular dilatation, valvular thickening with insufficiency or stenosis, aortic root diameter and coronary artery involvement should be performed.

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References