Actualities in Cardiac Disorders in Patients with Ankylosing Spondylitis

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Abstract

Spondyloarthritides are associated with increased cardiovascular risks, which can only partially be explained by traditional risk factors. It is likely that the chronic inflammatory state is involved. Spondyloarthritides, and in particular ankylosing spondylitis, are characterized by an excess mortality from cardiovascular disease - about 20-40%. The most specific lesions in patients with ankylosing spondylitis are aortic incompetence and conduction defects (first, second, and third degree atrioventricular block; bundle branch block; fascicular block; Wolff-Parkinson-White syndrome). The spectrum of cardiac pathologies is wide, and includes left ventricular dysfunction, mitral valve disease, aortic and mitral regurgitation, cardiomyopathy, pericarditis, aortic root dilatation, corpulmonale. Potential mechanisms for cardiac abnormalities comprise a chronic inflammatory condition with increased levels of circulating cytokines and acute phase reactants. Early detection of cardiac disorders in patients with ankylosing spondylitis, and particularly aortic valve disease and conduction disturbances, may have important therapeutic and prognostic implications.

Key words: seronegativespondyloarthritides, ankylosing spondylitis, aortic valve disease, conduction disturbances.

Актуальность поражения сердца у больных с анкилозирующим спондилоартритом

Спондилоартриты ассоциируются с высоким риском развития сердечно-сосудистых заболеваний, которые только частично объясняются традиционными факторами риска. Вероятно, что данная патология является следствием хронического системного воспалительного процесса. Спондилоартриты, в особенности анкилозирующий спондилоартрит, характеризуются высокой смертностью от сердечно-сосудистых заболеваний, которая составляет 20 - 40%. Наиболее специфичными поражениями являются аортальная недостаточность и нарушения проводимости (атриовентрикулярные блокады первой, второй и третьей степени; блокады ножек пучка Гисса; синдром Вольфа-Паркинсона-Уайта). Спектр сердечных патологий обширный и включает: дисфункцию левого желудочка, поражение митрального клапана, аортальную и митральную регургитацию, кардиомиопатии, перикардит, дилатацию корня аорты, легочное сердце. Потенциальные механизмы поражений сердца обусловлены хроническим воспалительным статусом и повышенным уровнем циркулирующих цитокинов и острофазовых реактантов. Своевременное определение сердечной патологии у пациентов с анкилозирующим спондилоартритом, в особенности поражение аортального клапана и нарушение проводимости, может существенно повлиять на лечение и прогноз данной категории больных.

Ключевые слова: серонегативные спондилоартриты, анкилозирующий спондилоартрит, поражение аортального клапана, нарушения проводимости.

Introduction

Seronegativespondyloarthritides are a related group of chronic inflammatory rheumatic diseases, encompassing ankylosing spondylitis, reactive arthritis, psoriatic arthritis, arthritis/ spondylitis with inflammatory bowel disease and a group of less defined, undifferentiated spondyloarthritides [1, 2]. Considering all spondyloarthritidis, the most common characteristics are asymmetric peripheral arthritis with predominant members inferred affecting, inflammation of the sacroiliac joints, inflammatory spinal pain, enthesitis, familial aggregation, association with the histocompatibility antigen HLA–B27 and seronegative for rheumatoid factor. This pathology presents a high incidence of extra-articular events, including the cardiovascular system, gastrointestinal tract, reticuloendothelial tissues, skin, mucous membranes, and eye damage. An important value in clinical manifestations of seronegativespondyloarthritides presents cardiovascular pathologies, which, in most cases, determines prognosis anddictates further tactics of treatment. Seronegativespondyloarthritides, especially ankylosing spondylitis, are associated with increased mortality from cardiovascular lesions (20-40%) [1].

Heart damage presents a well-known complication of ankylosing spondylitis.

Literature presents data that the most characteristic cardiac abnormalities in ankylosing spondylitis are aortic valve insufficiency and heart conduction disturbances. Pathologies have a wide-range, and may include mitral valve damage, cardiomyopathy and pericarditis [5, 6, 8]. For the first time, aortic valve damage was described by Mallory in 1936, and in 1951 Bauer drew attention to the association of aortitis and ankylosing spondylitis [4, 2]. The presence of aortic valve disease in a subgroup of patients with rheumatoid arthritis as a clinical manifestation has contributed to clarifying the distinction between rheumatoid spondylitis and ankylosing spondylitis as separate diseases [9].

Roldan studied the aortic root and valves in ankylosing spondylitis patients (n = 44) using transesophageal echocardiography (TEE), and found aortic root and valve disease in 82% of patients. Other irregularities were aortic root thickening, increased root stiffness and dilatation. Valve regurgitation was seen in about 50% of patients. It was also shown that aortic root and valve disease progressed over time and were associated with cardiovascular morbidity[4, 6].

Prevalence of aortic insufficiency advanced with age, disease duration, and presence of peripheral joint disruption. Graham and co-authors have shown a prevalence of 10.1% among patients who suffered ankylosingspondylitis for 30 years, compared with 1% of patients ill for five years. Prevalence has doubled in a subgroup of patients with peripheral joint damage (except femur and shoulder) [4, 9].

Aortitis was first described by Bulkley in 1973. Proximal aortic wall behind and above the Valsalva sinus, as supported by literature data, is thickened primarily due to healing and proliferation of adventitious. Vasa vasorum surrounded by plasma cells and lymphocytes, often making their stenosed lumen. Aortitis can extend below the aortic root to the base of mitral valve and interventricular septum inside. Scar tissue located below the mitral valve, according to scientists, results in a fibrous subaortic ridge. The inflammatory process is extended distally, usually by no more than a few centimeters within the ascending aorta, although there have been cases of larger expansions [4, 10].

Material and Methods

In our study, 137 patients were included with ankylosing spondylitis. The aim of the study provided for the peculiarities of damage to the heart in patients with ankylosing spondylitis. Tasks led to study in evaluating features of valvular damage, damage assessment of contractile function of the pericardium and ventricular myocardium, as well as estimating the degree of expression variations and disturbances of rhythm and conduction in such patients. Patients included in the study were undergoing extensive clinical examination. Using questionnaires of clinical diseases and laboratory explorations, the following were conducted: general analysis of blood, general analysis of urine, plasma glucose (glycemic profile), glycosylated hemoglobin (if necessary), profile lipid lipidograma, C-reactive protein, latex test, fibrinogen, coagulograma, transaminases, HLA-B27 determination. In all patients with ankylosing spondylitis, the following laboratory investigations were conducted: ECG in 12 standard derivatives, exercise stress test with dosed, the 24-48 hour Holter monitoring ECG, Doppler EchoCG.

Study exclusion criteria included patients younger than 18 and older than 60 years, diabetes type I or type II developed by the onset of the disease, dyslipidemia, congenital defects and rheumatic valvular disease, liver cirrhosis, obesity (BMI > 25 kg/m^2), treatment GCS-term (> 1 month) or > 1mg/kg/body (> 2 week).

Results and Discussion

Results of our study showed that the average age of patients was 43.5 ± 0.28 years, the duration of disease was 8.2 ± 0.33 years and the ratio of men to women was 6:1.

Aortic valve damage is proved in 1-10% of patients with ankylosing spondylitis [10]. Differences within subgroups of patients, such as age and disease duration may partially explain the variety of expression of these events. Aorta and aortic valve damage is usually a feature of disease duration in adults, although there have been cases in children. Graham aortic

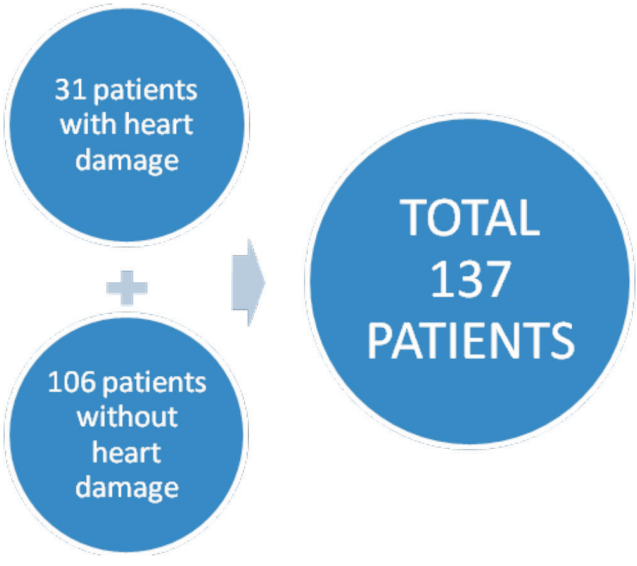

Fig. 1. Heart damage of patients with ankylosing spondylitis.

insufficiency detected only 21 of 519 ankylosing spondylitis patients compared with 3 of 508 - the control group with rheumatoid arthritis, and conduction abnormalities were present in 1-33%. Aortic valve damage in these varieties may be due to differences within the group of patients [5, 10].

According to the retrospective study we conducted, of the total 137 patients with ankylosing spondylitis, 31 of them have heart damage, which was 22.6% (fig. 1). Aortic valve damage occurred in eight patients, valvular insufficiency manifested by different degree preferred grade II and III (68%). In five patients with damage of the aortic valve (62.5%) echocardiographic data was recorded for aortosclerosis, which, according to the literature, is due to advancement in the atherogenic process persistent chronic systemic autoimmune inflammatory background [2, 10]. Aortosclerosis in these patients correlated significantly ($p < 0.01$) with ESR's growth of over 35 mm/h ($r = 0.98$), increased level of CRP ($r = 0.92$), fibrinogen over 4.5 ($r = 0.96$) (fig. 2).

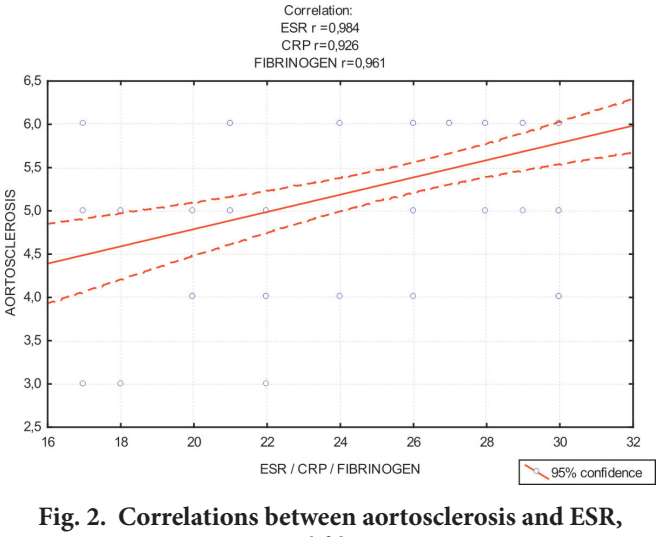

Fig. 2. Correlations between aortosclerosis and ESR, CRP and fibrinogen.

Thus, early detection of cardiac damage, particularly aortic valve damage, may have important prognostic and therapeutic aspects. Aortic root dilatation and the presence of a subaortic bump or ridge on the echocardiographic examination have been reported as evidence of preclinical aortic valve disease. Direct detection of aortic incompetence is now possible using Doppler echocardiography technique. Preclinical aortic incompetence was demonstrated in 2 recent studies [3, 7]. Prospective study using Doppler echocardiography extends our knowledge of the prevalence and results of aortic valve damage in ankylosing spondylitis and prognosis could help to predict the risk of severe valvular damage. Doppler echocardiographic examination of valve damage helps to identify patients at risk for endocarditis, such as those undergoing joint surgery.

Mitral regurgitation, supported by literature data, is uncommon but serious. Prevalence of mitral valve prolapse is higher than that found in the general population [6, 7].

Similarly, the prevalence of disorders expressed by atrioventricular block increased by 0.6% from disease progression after 5 years; 8.5% over 30 years [5]. In addition, the prevalence of aortic valve failure doubled when peripheral joints were affected. In our study, we found that 24 (77.4%) patients, 31 of those with heart disease, electrocardiographic and Holter monitoring, have resulted in intraventricular conduction abnormalities, of which 12 (38.7%) patients assessed the degree AV block I and II.

Because intracardiac conduction abnormalities may be transient, the frequency and duration of subsequent electrocardiographic monitoring investigations can play an important role. The prevalence of conduction disturbances is higher in patients with aortic valve damage. A wide variety of conduction defects were described, including first, second, and third degree atrioventricular block, bundle branch block, fascicular block, Wolf-Parkinson-White syndrome [1, 9]. Conduction disturbances pass spontaneously, even in cases of complete intracardiac blockage. Electrophysiological investigations in patients with intracardiac complete blockage, suggests that this block is localized preferentially in the atrioventricular node, although it is a possibly impaired conduction system [9].

Aortic insufficiency or disorders of conduction can be a clinical manifestation of ankylosingspondylitis. Bergfeld and colleagues completed a study which involved 223 patients with complete atrioventricular block, and found that in 7 of them that ankylosingspondylitis was present [1, 3, 7]. Eversemeyer and collaborators have found two patients with aortic valve damage, which after further investigations, spondiloarthritis was diagnosed with spondylitis [2, 5]. So, in the absence of other known causes of aortic insufficiency or conduction disturbances one should take into account the possibility of ankylosingspondylitis, particularly in younger men. The presence of cardiac symptoms depends on the location of pathology. Effort angina may occur, dyspnea, fatigue, or effort syncope Stokes-Adams attacks, but the clinical manifestation may be masked by ankylosingspondylitis. Chest pain can be interpreted as musculoskeletal pain rather than angina, and

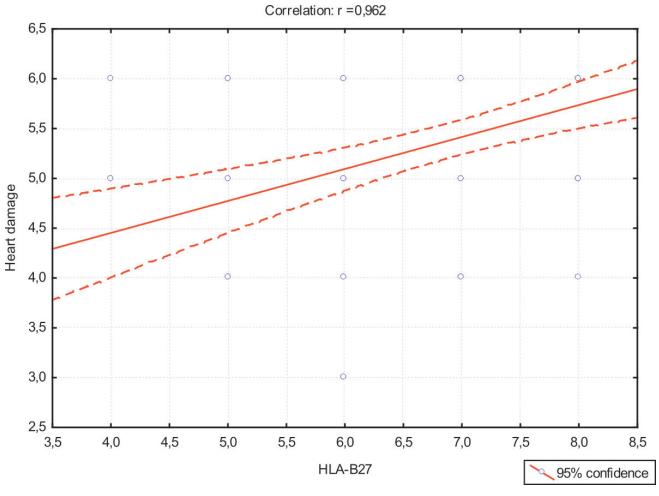

Fig. 3. Correlations between heart damage and HLA-B27 antigen.

dyspnea may be regarded as a manifestation of a musculoskeletal disability [3, 7].

Research conducted shows a slight increase in mortality of patients with ankylosingspondylitis, the effect being the main cause of cardiovascular death [8, 9, 10].

Current studies show no weight antigen HLA-B27 prevalence in patients suffering from aortic insufficiency, spondiloartritidis not affected by spondylitis. There is evidence, however, showing an increased incidence of HLA-B27 in men with complete heart block [10]. Our investigation revealed a close correlation between HLA-B27 antigen with cardiac pathology ($R = 0.96$, $p < 0.001$) (fig.3). Similarly, in these patients was assessed and an increased incidence of pleurisy, but may be due to duration of illness is associated with both diseases.

In recent years, emphasis has been placed on the recognition of ventricular myocardial damage in ankylosing spondylitis. Rebeiro has found that five of 28 patients with ankylosing spondylitis had dilated left ventricle and that its contractile function was disturbed [7, 8]. Brewerton showed impaired left ventricular diastolic function on echocardiography in 16 of 30 in male patients with ankylosing spondylitis who had

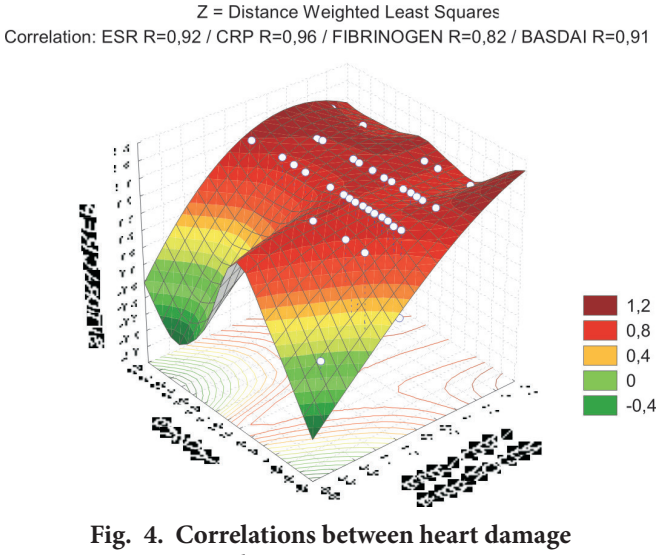

Fig. 4. Correlations between heart damage and HLA-B27 antigen.

cardiorespiratory symptoms or known heart disease [3, 8]. Conclusions were strengthened by the presence of excess tissue in the myocardium. Computerized image analysis of myocardial tissue obtained at necropsy of 28 patients showed the presence of interstitial reticulin 30.7%, versus 17.7% in the control group, depending upon age and gender ($p < 0.0001$).

Unlike rheumatoid arthritis in ankylosing spondylitis pericarditis has a clear clinical manifestation - both clinically and pathologically. Clinically evident pericarditis was only present in 2 of 222 patients with ankylosing spondylitis [3]. The retrospective study we conducted found only three patients with echocardiographic signs of pericarditis, which correlated with advanced levels of systemic inflammatory process. Determined corresponding to particular interdependence between pericarditis and ESR's value ($R = 0.92$, $p < 0.01$), CRP ($R = 0.96$, $p < 0.001$), BASDAI score ($R = 0.91$; $p < 0.01$) and fibrinogen ($R = 0.82$, $p < 0.05$) (fig. 4).

According to literature data, pericarditis is a more common clinical sign of Reiter's syndrome than in ankylosing spondylitis [5, 8, 9]. In patients with ankylosing spondylitis, there have been few cases of subacute bacterial endocarditis, which is surprising if one takes into account defects that predispose it [9]. It was also recorded in association with aortic arch syndrome ankylosing spondylitis [10]. Some authors describe the possible occurrence of pulmonary heart [4, 6].

Patients with angina pectoris require careful clinical examination in order to detect disturbances before administering β-blockers or calcium channel blockers, as they have an inhibitory effect on system management. Cardiostimulating proved effective in treating symptoms of intracardiac block, but in asymptomatic patients may be taken and tactical surveillance [4, 9]. Patients with heart disease exercise should continue to maintain posture and spinal mobility, and all patients with valvular lesions should be informed about methods of prevention of subacute bacterial endocarditis [10].

Conclusions

Thus, cardiovascular pathology in ankylosing spondylitis is polymorphic and a significantly worse prognosis. Knowledge of the genesis of cardiovascular diseases in ankylosing spondylitis is limited: unknown trigger antigen pathogenetic mechanisms of development of inflammation in the wall of the aorta and the aortic valve is not clear, because of selective involvement in pathological process of left ventricular myocardial muscle and its impact on immune system. In our study, patients with significant frequency have been manifested by valvular heart impairment (particularly aortic), disorders of intraventricular conduction and exsudative pericarditis. They are expressed in such patients who have not received adequate medical treatment, or when medication was abandoned. It was significantly expressed in systemic inflammatory syndrome, which closely correlated with the degree of cardiac involvement. Prospect characterizations of cardiovascular damage in these patients will cause irreversible change by targeting of the correct diagnosis and will improve prognosis in these patients.

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