PAINLESS CARDIAC ISCHEMIA AND RHEUMATOID ARTHRIT

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ABSTRACT

Rheumatoid arthritis (RA) is an autoimmune rheumatic disease of unknown etiology characterized by chronic erosive arthritis and systemic inflammatory damage to internal organs. In Uzbekistan, RA affects about 1.5% of the entire adult population. RA most often affects people aged 30-50 years. Women get sick 5 times more often than men. The main cause of mortality in RA are cardiovascular catastrophes (myocardial infarction (MI), cerebral stroke (CS) den cardiac death (SCD)). According to a meta-analysis of prospective studies, the risk of cardiovascular mortality in RA is 60% higher than in the general population. Cardiovascular complications (CVD) caused by atherosclerotic vascular lesion in RA have features characterized by multiple coronary vascular lesions; early relapses of acute coronary syndrome; increased mortality after the first MI and a high frequency of "asymptomatic" MI (relative risk (HR) – 2.13). The problem of coronary heart disease (CHD) and its complications in patients with rheumatoid arthritis (RA) is widely discussed in the literature. And this is not accidental. In the structure of the causes of premature mortality in RA, the largest share falls on coronary heart disease and its complications. Epidemiological studies have shown a high incidence of myocardial infarction and sudden coronary death in RA patients. At the same time, the relative risk (RR) exceeded the general population indicators by more than 2 times. In patients with coronary heart disease, the presence of rheumatoid arthritis is associated with a significant increase in the 10-year risk of myocardial infarction, major adverse cardiovascular events and death from all causes. Representatives of immuno-inflammatory diseases are rheumatic diseases, primarily rheumatoid arthritis, juvenile idiopathic arthritis, spondyloarthritis, psoriatic arthritis, gouty arthritis, systemic lupus erythematosus and other systemic connective tissue diseases, which are characterized by a high risk of premature death of patients. It has been established that the high risk of premature death in these diseases is associated with the "severity" of the immuno-inflammatory process, leading to severe irreversible damage to vital organs and systems, and with the development of a wide range of combined conditions (infections, interstitial lung disease, malignant neoplasms, osteoporetic fractures, etc.). Among them, the central place is occupied by pathology of the cardiovascular system, most often caused by the early development and accelerated progression of atherosclerotic lesions of coronary vessels. The article presents the literature data of recent years concerning the effect of antirheumatic therapy (basic anti-inflammatory and genetically engineered biological drugs) on the cardiovascular system

Keywords: rheumatoid arthritis, coronary heart disease

INTRODUCTION

To date, information has been accumulated about possible causal relationships between the activity of inflammation and the accelerated progression of atherosclerosis, which is undoubtedly relevant in RA. According to the results of epidemiological studies, RA is recognized as an independent predictor of coronary heart disease in the general population. Asymptomatic atypical course of acute coronary syndrome was observed in every 5th RA patient. Almost half of the patients with RA were found to have painless ischemia based on the results of daily ECG monitoring. According to some data, pain-free ischemia occurred in 45% of RA patients, while a significant frequency (82.5%) of rhythm disturbances was noted, mostly due to supraventricular extrasystole in association with inflammatory activity. Perfusion single-photon emission computed tomography under pharmacological stress revealed signs of stable coronary heart disease in 59% of RA patients and 27% of the examined control group. Multivessel atherosclerotic lesion of the coronary arteries was diagnosed in a large number of patients with RA by coronary angiography. The causal relationship of endothelial dysfunction, the progression of which occurred in parallel with an increase in the activity of immunopathological inflammation, and the accelerated development of coronary atherosclerosis in RA patients was demonstrated by V.I. Mazurov et al. At the same time, the traditional risk factors – arterial hypertension (AH) and hypercholesterolemia – were less important in the formation and progression of coronary heart disease in this category of patients.

Interestingly, a comparative pathohistological examination of coronary vessels in RA patients and in the control group in the clinic did not reveal significant differences in the frequency and severity of stenoses. Critical stenoses of the III–IV degree were more often found in patients without RA (54%) than in patients with RA (7%; p=0.023), which contradicted the data of numerous studies. At the same time, only a high frequency of unstable "vulnerable" plaques in RA was convincingly demonstrated in comparison with the control (48 and 22%, p=0.018), which confirmed the possible key role of inflammation in the progression of atherosclerosis and its complications. A case of reverse development of stress-induced myocardial ischemia (according to myocardial scintigraphy) was described against the background of immunosuppressive therapy in a 62-year-old RA patient with unchanged coronary arteries according to angiography. The authors suggested that ischemia could be caused to a greater extent by endothelial dysfunction and microcirculatory disorders due to chronic inflammation. The formation in patients has been repeatedly noted RA atherogenic profile of the lipid spectrum in the form of reduced cholesterol (HC) of high-density lipoproteins (HDL) in combination with hypertriglyceridemia. The severity of dyslipidemia in patients with RA was associated to a greater extent with the duration and activity of inflammation. It is important to emphasize the inverse correlation of HDL cholesterol levels with classical markers of inflammation, such as CRP and ESR. The disease-modifying therapy of RA, aimed at suppressing the activity of inflammation and slowing the progression of joint destruction, was often associated with an increase in HDL levels, which means it could have potentially anti-atherogenic properties.

The purpose of our study is to study the frequency, structure and features of the

course of coronary heart disease in RA.

MATERIALS AND METHODS

An analytical one-stage cross-sectional study of cardiovascular pathology was conducted in 77 patients with RA in a representative sample of Samarkand patients. Women prevailed (19 or 81.3%) with a moderate degree of activity according to DAS 28 (4.4±1.9), seropositivity according to RF (51 or 81.3%) and the III radiological stage of the disease (8 or 44.0%). Functional insufficiency of the joints corresponded in the overwhelming majority of cases to the II–III functional class. The average age of patients was 55.4±11.6 years, the duration of RA was 14.7 (2; 20) years. The diagnosis of coronary heart disease was verified on the basis of clinical, laboratory and instrumental data. All patients underwent an ECG in 12 standard leads for device Schiller AT-10 Plus (Schiller, Switzerland) and daily monitoring of blood pressure and ECG according to the generally accepted method using bifunctional monitors Cardio Tens-01 and Meditech card(x)plore (Hungary). The level of serum lipids was determined by the enzymatic method on an automatic analyzer In / M HITACHI 902 (Roche B/M, France). Endothelial function was assessed noninvasively using vasodilation tests by D.S. Celermajer. Statistical processing of the results was carried out using Epi info ver.6, Biostatistica 4.0 McGraw – Hill, Statistica application software packages 6.0 (Statsoft, USA).

RESULTS

Coronary heart disease in RA after detailed verification of the diagnosis, taking into account daily ECG monitoring, was detected in 35 (45.9%) patients: typical angina pectoris was in 19 (52.5%), pain–free ischemia and rhythm disturbance - in 9 (25.4%) and 7 (22.1%) patients, respectively. At the same time, a high proportion of vertebrogenic cardialgia was noted – in 30 (48.8%) patients from among those who complained of pain in the heart area. This may create prerequisites for the erroneous interpretation of chest pain in this category of patients. In the vast majority of cases, cardialgia was diagnosed in postmenopausal women (88% vs. 12% in men, $p<0.01$), long–term RA patients (15.6±7.6 years), who in a large number of cases (41%) were prescribed glucocorticoids - GC (41%), including in the form of intra-articular injections (on average 7.5± 1.5 injections per year). This does not exclude the possible development of osteopenic syndrome in their spine and related complications.

Detailed verification of the diagnosis of coronary heart disease was carried out by daily monitoring of an ECG diagnostic test alternative to a physical exercise test due to functional insufficiency of the joints in this category of patients. A comparative characteristic of the pathology detected during daily monitoring of ECG and resting ECG is presented in Table 1.

The method of daily ECG monitoring in RA patients made it possible to reliably verify ischemic changes, atrial fibrillation and atrioventricular conduction disorders more often than resting ECG, which must be taken into account in a wide clinical practice.

Significant risk factors for coronary heart disease in RA patients, according to the results of logistic regression, are presented in Table 2 in rating order.

From the data in Table. 2 it can be seen that the risk of coronary heart disease in RA increased significantly when combined with traditional cardiovascular risk factors

– hypertension, smoking and anemia, early menopause in women, decreased GFR, burdened with heredity for cardiovascular diseases (CVD), overweight, high average daily heart rate, atherogenic profile dyslipidemia and hyperglycemia. Along with traditional predictors of cardiovascular risk, the contribution of factors associated with RA has been demonstrated. Thus, long–term use of GC and high activity of inflammation according to DAS 28 increased the risk of coronary heart disease in this category of patients by 5 and 3.5 times, respectively (5.06-2.66<HR<9.54, p<0.01 and 3.67– 1.93<HR<7.01, p<0.01).

Table 1. Structure of pathology detected during resting ECG and daily ECG monitoring

Pathology	ECG		p (by $\chi 2$)
	rest	daily monitoring	
Ischemia*	**10 (13,6)**	**18 (23,7)**	**0,004**
Postinfarction Cardiosclerosis**	**7 (8,9)**	**7 (8,9)**	**1,0**
Atrial fibrillation	**16 (21)**	**22 (28,8)**	**0,04**
Blockade Of The LLGB	**5 (7)**	**5 (7)**	**1,0**
Blockade of the anterior LLGB	**10 (12,8)**	**10 (12,8)**	**1,0**
Atrioventricular blockades	**4 (5)**	**10 (12,8)**	**0,004**
Extrasystole	**26 (34)**	**29 (37,7)**	**0,4**

Note. In parentheses – the percentage of patients (here and in Table 2). LDL – the left leg of the Gis bundle; * – ischemic changes in the terminal part of the ventricular complex – the ST segment and the T wave. Criteria for myocardial ischemia were considered horizontal or oblique depressions of the ST segment > 1 mm 0.08 s after the end of the QRS complex (point J) duration 1 min; Postinfarction Cardiosclerosis**– signs of a myocardial infarction.

Among RA patients with an established diagnosis of coronary heart disease, the frequency of endothelial dysfunction was 86.4% (n=31). As is known, the clinical equivalent of endothelial dysfunction is a tendency to vasoconstriction. In 9 patients with pain-free ischemia, endothelial dysfunction was found in the vast majority of cases (93%), which suggests that they have a close pathophysiological relationship of ischemia with vasospastic reactions.

The analysis of the lipid spectrum did not reveal a dominant hypertriglyceridemia and/or a predominant decrease in HDL levels, as previously shown in some studies. Thus, the average level of total CHOLESTEROL was 5.0± 1.9 mmol / l, LDL cholesterol – 3.0± 0.9 mmol / l, HDL cholesterol – 0.9± 0.3 mmol / L, triglycerides – 1.6± 0.5 mmol / l, the frequency of isolated hypercholesterolemia – 29.6%, various variants of dyslipidemia – 34.2%.

Table 2. Risk factors of coronary heart disease in RA patients

Sign	RA		OP	p (by $\chi 2$)
	with CHD (n=118)	without CHD (n=139)		
FROM>88 cm (w.), 102 cm (m.)	17 (48,3)	15 (35,9)	1,66 (0,98<OP<2,83)	0,045
Age > 50 years	18 (50,8)	16 (38,1)	1,68 (0,99<OP<2,85)	0,04
Reception of the GC	17 (49,2)	13 (32,4)	2,02 (1,18<OP<3,46)	0,009
Hyperglycemia or with DM	7 (21,2)	5 (11,5)	2,07 (0,99<OP<4,33)	0,03
Morning stiffness >120 min	16 (45,8)	12 (28,8)	2,09 (1,21<OP<3,62)	0,007
Total HC >5.0 mmol/L	13 (38,1)	9 (22,3)	2,15 (1,20<OP<3,85)	0,008
Duration of RA >10 years	27 (76,3)	25 (59)	2,23 (1,26<OP<3,99)	0,005
LDL CHOLESTEROL >3.0 mmol/l	16 (44,1)	11 (25,9)	2,25 (1,29<OP<3,95)	0,0034
Heart rate-24 > 70 beats/min	16 (44,1)	10 (25,2)	2,34 (1,34<OP<4,11)	0,002
BMI>25 kg/m2	17 (48,3)	11 (27,3)	2,48 (1,43<OP<4,32)	0,0
DAS >50 mm	18 (50,8)	12 (28,8)	2,56 (1,48<OP<4,43)	0,0004
Heredity by CVD	15 (42,4)	8 (19,4)	3,05 (1,69<OP<5,54)	0,0001
Total dose of HA (prednisone) >3 g	13 (38,1)	7 (16,5)	3,11 (1,67<OP<5,80)	0,0001
The daily dose of prednisone is >7.5 mg / day	9 (25,4)	4 (9,4)	3,30 (1,55<OP<7,12)	0,0
Decrease in GFR <60 ml/min	26 (72,9)	18 (43,1)	3,54 (2,02<OP<6,21)	0,0
Menopause up to 45 years	8 (23,7)	4 (7,9)	3,62 (1,63<OP<8,2)	0,0008
High activity on DAS28	9 (38,1)	6 (14,4)	3,67 (1,93<OP<7,01)	0,0
Anemia	8 (23,7)	3 (6,5)	4,71 (2,01<OP<11,3)	0,0
Duration of GC intake >12months	16 (45,8)	6 (14,4)	5,02 (2,66<OP<9,54)	0,0
Smoking	7 (18,6)	1 (2,2)	10,2 (2,84<OP<44,9)	0,0
Frequency of AG	29 (83,1)	12 (28,8)	12,1 (6,39<OP<23,3)	0,0

Note. OT – waist size; DM – diabetes mellitus; LDL – low density lipoproteins; HR-24 – average daily heart rate according to daily ECG monitoring; BMI – body mass index; GFR – glomerular filtration rate.

Thus, CHD, according to our observations, was established in 45.9% of RA

patients. The features of the course of this pathology include frequent detection of rhythm disturbances and pain-free ischemia. Routine diagnostic methods, both clinical and instrumental, do not always allow to confirm the diagnosis of coronary heart disease in this category of patients. This is due to the high frequency of cardialgia, which can contribute to erroneous diagnosis. The inability to use the test with physical activity significantly limits diagnostic capabilities, therefore, other diagnostic tests should be used more widely, in particular daily ECG monitoring. The high frequency of endothelial dysfunction with a tendency to vasoconstriction, especially in pain-free ischemia, should be taken into account in clinical practice. Such patients are necessarily prescribed antagonists of slow calcium channels and beta-blockers with a vasodilating effect. Significant risk factors for coronary heart disease (along with traditional ones) directly associated with the consequences of chronic inflammation are the activity and duration of RA, your pain >50 mm, taking HA > 12 months in a total dose of > 3 g in terms of prednisone, as well as concomitant anemia as a frequent complication of RA.

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