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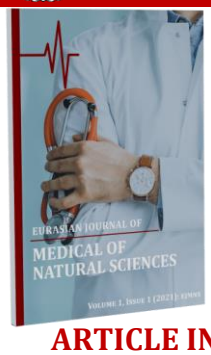

SYSTEMIC LUPUS ERYTHEMATOSUS AND CARDIOVASCULAR PATHOLOGY

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ABSTRACT

Systemic lupus erythematosus, sometimes known as SLE, is a type of autoimmune illness that can express itself in a dizzying array of different ways in patients. Atherosclerosis and the conditions that result from it are the leading causes of late mortality in people who have complications from SLE. Traditional risk factors, the presence of specific risk factors, the duration of the course, the use of glucocorticoids (GC), the presence of autoantibodies to double-stranded (native) DNA, and the presence of antiphospholipid antibodies all create conditions that accelerate the development of atherosclerosis in this group of patients. The research that is now available suggests that established risk factors for cardiovascular disease should be revised in order to take into consideration the beneficial effect of antimalarial medications as well as the unfavorable prognostic effect of prolonged use of GC.

Introduction. Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with an extremely broad spectrum of clinical manifestations (1). The prevalence of SLE is relatively low in various European countries, estimated between 25 and 39 cases per 100,000 population, yet the disease is of great social importance due to its severe and often unpredictable course, predominantly affecting young adults, and high mortality rates [2]. In recent decades, significant progress has been made in the treatment of SLE, due to the successful introduction of high-dose glucocorticoids (GCs), including pulse therapy with methylprednisolone, modern cytostatic regimens, haemodialysis and renal transplantation.

In XXI century 15-year survival rate in SLE increased up to 85%, but insufficient control of disease activity, necessity of practically constant intake (GC) and immunosuppressive drugs lead to accumulation of irreversible (accrul) inner organ damage and, as a result, decrease of life quality, disability, social disadaptation, premature lethality [3]. At the same time, "early" mortality is associated with the activity of immunopathological process and infectious complications, while "late" mortality - cardiovascular complications due to atherosclerotic vascular lesions [4].

Cardiovascular disease (CVD) as a cause of mortality in patients with HSCLC ranges from 4 to 76% according to different authors [5]. According to studies, the prevalence of CVD in patients with SLE, despite the relatively young average age of patients (30-45 years) and the

prevalence of women among patients, is 6%-10%, and the annual incidence is 1.5%. The cardiovascular risk in the Pittsburgh cohort of patients with SLE was 5-6 times higher compared with patients in the well-known Framingham study. In women aged 35-44 years with SLE, the incidence of cardiovascular events (CVE) was 50 times higher than in the control group [6]. A Swedish rheumatology study that followed 86 adult patients with SLE over 6 years found a 9-fold increase in the incidence of MI compared to the general population [7,16].Underlying the increased cardiovascular risk in SLE is the accelerated development of atherosclerotic process. Many studies investigating markers of preclinical atherosclerosis of peripheral arteries in rheumatic diseases demonstrate a more pronounced prevalence and severity of such predictors of future cardiovascular accidents, such as carotid intima-media complex (CMC) thickening, endothelial dysfunction (ED), decreased elasticity of the arterial wall, the presence of atherosclerotic plaques (AB) in peripheral arteries and calcifications in coronary arteries [8].

Clinical manifestations of atherosclerosis (angina, MI, cerebral and peripheral artery disease) occur in about 20% of patients. The average age of onset of MI in patients with SLE is 49 years, which is 20 years less than in the general population. Subclinical forms of the disease are much more common, occurring in 35-40% of patients [9]. The classic risk factors for CVD in SLE are similar to those in the general population: dyslipidemia, diabetes mellitus (DM), smoking, obesity, arterial hypertension (AH), age, sedentary lifestyle, hereditary CVD, etc. Recent studies have shown a significant increase in the incidence of MI and stroke in patients with SLE, so the disease itself and its treatment are recognized as likely risk factors for cardiovascular damage [10]. A number of studies associate accelerated development of atherosclerosis with the activity and duration of the disease, the severity of internal organ damage, the cumulative dose of HC, the presence of nephritis, and increased antibodies to cardiolipin [17].

One possible explanation for the accelerated course of atherosclerosis and related diseases in patients with SLE seems to be the increased expression and frequency of the known "classic" cardiovascular risk factors. Indeed, given the frequent involvement of the kidneys in the pathological process, reduced physical activity, the use of HC and nonsteroidal anti-inflammatory drugs, as well as the earlier onset of menopause, it is reasonable to expect increased expression of AH, lipid spectrum disorders and DM in patients with SLE.

In recent decades, the views on atherosclerotic disease have undergone significant changes, its pathogenesis is no longer presented as a simple consequence of lipid accumulation in the arterial walls, but instead is seen as a complex process involving many metabolic, microstructural, inflammatory and even immune changes. The primary link in the chain of pathological changes in atherosclerotic disease is currently considered to be ED induced by various risk factors such as smoking, LH, DM, exposure of the vascular wall to LDL and LDL-C. HDL usually play a protective role in atherosclerosis by reversing cholesterol transport and protecting LDL from oxidation. However, in CVD, so-called proinflammatory HDL is found in 45% of patients, and its presence correlates with increased formation of oxidized LDL, the number of carotid atherosclerotic plaques and increased CMD thickness [11]. In addition to traditional CVD risk factors, the association between SLE and atherosclerosis may be due to additional risk factors - inflammation and autoimmune

processes [18]. In SLE, antiphospholipid antibodies also play an important role in increasing the risk of adverse CVD and accelerating atherosclerosis, provoking I-cell-mediated inflammation of the vascular wall with subsequent activation of Hagemann factor and platelet aggregation, leading to increased uptake of oxidised LDL by macrophages and being a major factor in unstable LB and thrombotic complications [12].

In recent years, much attention has been paid to type 1 interferons (IFN I) as an important mediator of SLE pathogenesis. IFN I has been shown to be capable of initiating endothelial damage and the formation of atheromas, the presence of which correlates with SLE activity. In 2004, a new form of programmed cell death - neutrophil extracellular trap (NVL) formation - was described [13]. EFLs are extracellular chromatin combined with neutrophil proteins and are designed to "trap" and destroy pathogens. Impaired NVL formation has been noted in patients with SLE. Neutrophils in SLE have an increased ability to form VVLs that stimulate the production of IFN1 and autoantibodies such as anti-cytheli-cidin-Eb37 and anti-ribonucleoprotein; in addition, lupus neutrophils are able to secrete VVLs that have a damaging effect on endothelium in vitro [14].

Drugs also influence the rate of progression of atherosclerotic disease in patients with SLE. On the one hand, the use of GC, cytostatics, mycophenolatamofetil and anti-B-lymphocyte drugs can reduce the activity of systemic inflammatory process and weaken its impact on the progression of atherosclerotic disease, but on the other hand, GC, especially their high doses can lead to hyperexpression of traditional risk factors of atherosclerosis. In order to attenuate the negative effects of HAs on the cardiovascular system, it is important to aim for the lowest effective maintenance dose when achieving their anti-inflammatory effect.

Currently, there are obtained data on favorable effect of aminoquinolone derivatives on atherosclerotic disease risk in SLE based on the ability of hydroxychloroquine and chloroquine to decrease LDL level and increase HDL level, decrease proco-agulation properties of blood serum of SLE patients and production of antiphospholipid antibodies [15]. The positive effect of methotrexate in the prevention of CVD in RA patients is widely known. However, the available data do not allow conclusions to be drawn regarding the protective effect of methotrexate on the development of CVD in RA. Statins may play a role in preventing the accelerated development of atherosclerosis in RA. Their use leads to a reduction of prothrombotic factors in ASF and a reduction of cardiovascular complications in patients with SLE [19]. They also have immunomodulatory effects. Treatment of patients with SLE with fluvastatin for 1 month reduced SLEDAI activity index, lipid levels, oxidative stress and vascular inflammation [20].

Thus, atherosclerosis and its complications are the main cause of late mortality in patients with SLE. SLE and CHD share common pathophysiological mechanisms associated with systemic chronic inflammation. At the same time, traditional risk factors cannot fully explain the mechanism of accelerated atherosclerosis in SLE. The presence of specific risk factors, such as duration of course, GC use, presence of autoantibodies to double-stranded (native) DNA and AFA, create conditions for accelerated development of atherosclerosis in this group of patients. Further research should help to develop effective risk scales and specific therapeutic programmes for the prevention and treatment of CVD in patients with SLE.

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