

Accelerated atherosclerosis in autoimmune rheumatic diseases

Otoimmün romatizmal hastalıklarda hızlanmış damar sertleşmesi

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ABSTRACT

Atherosclerosis is increasingly considered an immune system-mediated process of the vascular system. Autoantibodies, autoantigens, pro-inflammatory cytokines and infectious agents play a role in that process. Autoimmunity-related cardiovascular disease and atherosclerosis are important clinical problems. The reason for accelerated atherosclerosis in patients with autoimmune rheumatic diseases remains unclear. Some cases of autoimmunity-related cardiovascular disease may be more related to thrombosis than atherosclerosis. Although, mechanisms causing the increased risk are not precisely clarified, a combination of traditional and nontraditional risk factors, including inflammation appears to be of importance. Further studies are needed to determine whether these autoimmune rheumatic diseases are also associated with accelerated atherosclerosis and its manifestations. *J Clin Exp Invest* 2010; 1(3): 232-234

Key words: Atherosclerosis, autoimmune rheumatic diseases, mechanisms

INTRODUCTION

The mechanisms for the assumed accelerated atherosclerosis in autoimmune rheumatic diseases such as systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis include the classical risk factors, but may also be due to chronic inflammatory processes and immune dysregulation.^{1,2} This phenomenon can be attributed to the traditional risk factors for atherosclerosis and use of specific drugs, such as corticosteroids, but also may be the result of other autoimmune and inflammatory mechanisms that are aggravated in autoimmune rheumatic diseases.^{3,4} Several autoantibodies are associated with athero-

ÖZET

Ateroskleroz artan bir şekilde dammar sisteminin immune system aracılı bir oluşumu olarak algılanmaktadır. Otoantikorlar, otoantijenler, yangı artırıcı sitokinler ve enfeksiyöz etkenler bu oluşumda rol alabilir. Otoimmünite bağlantılı kalp-damar hastalıkları ve damar sertliği önemli klinik sorunlardır. Otoimmün romatizmal hastalıklarda hızlanmış damar sertliği gelişmesinin nedeni açık değildir. Bazı otoimmünite ilişkili kalp-damar sorunları damar sertliğinden ziyade tromboz ile ilişkilidir. Artan riskin mekanizmaları net olarak açıklanmamakla birlikte, geleneksel olan ve olmayan risk faktörlerinin - yangı da içlerinde olarak - bir kombinasyonu önemli gözükmetedir. Otoimmün romatizmal hastalıkların hızlanmış damar sertleşmesi ve belirtileri ile birlikte olup olmadığı konusunda yeni araştırmalara gereksinim vardır. *Klin Den Ar Derg* 2010; 1(3): 232-234

Anahtar kelimeler: Damar sertliği, otoimmün hastalıklar, mekanizmalar

sclerosis and its manifestations in humans. The antibody levels were higher in those patient groups than in control subjects.^{5,6}

Accelerated atherosclerosis in rheumatoid arthritis

Several types of cardiac involvement can occur in rheumatoid arthritis (RA). RA itself seems to represent a significant risk factor for development of early atherosclerosis and cardiovascular diseases (CVD).⁷⁻⁹ RA treatment and lifestyle of RA patients may favor physical inactivity, hypertension, diabetes mellitus, and obesity, but there is no clear

evidence that these factors are implicated in accelerated atherosclerosis in RA.¹⁰⁻¹² Despite the fact that different factors could alter endothelium homeostasis, prevalent data support the view that abnormal endothelial function in RA is essentially linked to inflammation.^{13,14}

Accelerated atherosclerosis in SLE

Although atherosclerosis develops early in the course of the disease, older age at diagnosis seems to be the major determinant of atherosclerosis in SLE.¹⁵ Among the nontraditional risk factors, cumulative dosage and/or longer duration of corticosteroid therapy and longer duration of disease seem to be the major predictors of atherosclerosis in SLE studies.¹⁶ The evaluation of risk factors for clinical atherosclerosis is difficult in SLE, since there are few observed cardiovascular events because of low prevalence of the disease.¹⁷ Whether premature atherosclerosis is a general feature of autoimmune diseases such as SLE or only affects a subgroup of patients whereas others do not have an increased risk remains to be demonstrated.¹⁸

Accelerated atherosclerosis in antiphospholipid syndrome

The pathogenesis of accelerated atherosclerosis in APS may be a result of an interaction between traditional and nontraditional risk factors.¹⁹ Thrombophilia may be associated with premature atherosclerosis, and accelerated atherosclerosis was suggested as an additional clinical feature of APS.²⁰ This pathological process may be mediated by the direct proinflammatory and procoagulant activity that anti-phospholipid antibodies (aPLs) exert on endothelial cells or indirectly, via the inflammatory immune mechanisms that have been implicated in autoantibody-mediated thrombosis.²¹ Further studies are needed to determine whether atherosclerotic plaques in autoimmune disease have special features or whether systemic factors such as aPLs trigger atherothrombosis more easily than in normal atherosclerosis.²²

Accelerated atherosclerosis in systemic sclerosis

Systemic sclerosis affects the microcirculation and injures the endothelium, leading eventually to vessel occlusion and tissue anoxia.²³ In addition, systemic sclerosis significantly accelerates the sufferance of

the vessel wall of the macrocirculation, increasing the risk of vascular occlusive diseases. Extend of enhanced atherosclerosis in systemic sclerosis is not yet clear, because fewer studies compared with those of RA, SLE, and APS.²⁴

Primary systemic vasculitis and accelerated atherosclerosis

Many similarities exist between atherosclerosis and primary systemic vasculitis with respect to the initial localization, the role of multiple causal factors and pathogenetic mechanisms, and some clinical manifestations and possible future treatment strategies.²⁵ Vessel intima is the site at which inflammation develops in atherosclerosis and in most types of primary systemic vasculitis.²⁶ Vasculitis may trigger or favor not only inflammatory but also immune reactions associated with atherogenesis, for example, increasing the expression of autoantigens on activated endothelial cells.^{27,28}

Atherosclerosis in Sjögren's syndrome

Cardiac involvement is very rare among patients having Sjögren's syndrome.³ Currently there is no available data suggesting that this common autoimmune condition is associated with enhanced atherosclerosis. The data suggest that further studies are indicated to determine the risk of atherosclerosis among patients with Sjögren's syndrome.^{5,6}

Conclusions

Enhanced and premature atherosclerosis is a feature of some autoimmune rheumatic diseases and a possible feature of others because of inflammation and more specific immune mechanisms. The risk of cardiovascular disease is very high in SLE and also increased in RA and most likely to a varying degree in other autoimmune disease. However, it is not clearly established that the increased risk is present in most if not all patients, or only affects a smaller subgroup of patients.

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