Karolinska Institutet

Institutionen för Medicin, Huddinge, Enheten för Reumatologi

Studies of Atherosclerosis in Systemic Lupus Erythematosus

AKADEMISK AVHANDLING
som för avläggande av medicine licentiatexamen vid Karolinska Institutet offentligen försvaras i Kursrum 8, R63, Karolinska universitetssjukhuset i Huddinge

Fredagen den 23 september 2011, kl 10.00

av

Cristina Anania
leg. läkare

Huvudhandledare:
Professor Johan Frostegård
Karolinska Institutet
Institutet för miljömedicin
Enheten för immunologi och kronisk sjukdom

Bihandledare:
Professor Ingiäld Hafström
Karolinska Institutet
Institutionen för medicin Huddinge
Enheten för reumatologi

Professor Ulf de Faire
Karolinska Institutet
Institutet för miljömedicin
Enheten för kardiovaskulär epidemiologi

Med. dr. Mikael Heimburger
Karolinska Institutet
Institutionen för medicin Huddinge,
Enheten för reumatologi

Betygsnämnd:
Professor Lena Jonasson
Linköpings universitet,
Institutionen för medicin och hälsa
Avdelningen för kardiovaskulär medicin

Professor Ronald van Vollenhoven
Karolinska Insitutet
Institutionen för medicin Solna
Enheten för klinisk behandlingsforskning, inflammationssjukdomar

Docent Per Larsson
Karolinska Institutet
Institutionen för medicin Huddinge
Enheten för reumatologi

Stockholm 2011

ABSTRACT

The role of inflammation in the development of atherosclerosis is now accepted and a focus of many studies because of its complex mechanisms. The risk of cardiovascular disease (CVD) and atherosclerosis is reported to be increased in systemic lupus erythematosus (SLE), especially in the group of young women. The introduction of statins in the 1990's lowered considerably the morbidity and mortality in CVD. In the last decade, research efforts were concentrated on the immunological mechanisms of atherosclerosis and on the possibility to influence these mechanisms.

Our group recently reported a negative association between natural IgM-antibodies against phosphorylcholine (IgM anti-PC) and CVD outcome in the general population. Potential mechanisms considered include anti-inflammatory properties and inhibition of uptake of oxidized low density lipoprotein (oxLDL) in macrophages. The objective herein was to study mechanisms of atherosclerosis in SLE and the relation to traditional and non-traditional risk factors in an SLE cohort, in comparison with an age and sex matched control group. As systemic endothelial dysfunction is one of the earliest signs of atherosclerosis in the general population, we also assessed skin microvascular endothelial function in SLE patients and controls.

A total of 114 patients with SLE were compared with 122 age and sex-matched population-based controls. Common carotid intima-media thickness (IMT), calculated intima-media area (cIMa) and plaque occurrence were determined by B-mode ultrasound. Plaques were graded according to echogenicity. Anti-PC was assessed by enzyme-linked immunosorbent assay (ELISA). Endothelial function in skin was tested with local application of acetylcholine (ACh) and any concomitant increase in skin perfusion was measured with Laser Doppler Fluxmetry (LDF) in 84 of the SLE-patients and 81 of the age- and sex-matched controls.

Incidence of hypertension, presence of insulin resistance (determined by homeostasis model assessment of insulin resistance, HOMA-IR) and the levels of triglycerides and C-reactive protein (CRP) were increased in the SLE patients, while smoking, cholesterol and high density lipoprotein (HDL) did not differ from controls. Low levels of IgM anti-PC were more common in the SLE patients than in the controls. IMT and cIMa did not differ significantly between groups. However, plaques were more often found in the SLE patients. Age, LDL and IgM anti-PC were independently associated with plaque occurrence in the SLE patients. Furthermore, in the left carotid arteries echolucent plaques were more prevalent in SLE when compared to controls. There were no significant differences in skin microvascular endothelial function between SLE patients and controls. In the SLE group, endothelial function did not vary in relation to presence of skin manifestations, Raynaud's phenomenon, nephritis or plaque occurrence. In SLE patients with CVD, however, endothelial function was impaired.

Conclusion: Plaque occurrence in the carotid arteries was increased in SLE and was independently associated with age, LDL and low anti-PC levels. Vulnerable plaques were more common in SLE than in controls. Anti-PC could be a novel risk marker for atherosclerosis with therapeutic potential in SLE. Skin microvascular endothelial function was associated with CVD but not with early signs of atherosclerosis in SLE-patients. The endothelial function was not different in SLE-patients, as compared to controls.