SUMMARY OF PhD THESIS

The role of anti-oxLDL autoantibody-mediated processes in association with immune mechanisms of atherothrombotic diseases

Renata Laczik MD

3rd Department of Internal Medicine
University of Debrecen

Tutor: Pál Soltész MD PhD DSci

Kálmán Laki Doctoral School

(Cardiovascular diseases program)

We investigated immune processes induced by oxidized LDL on mononuclear cells separated from patients with antiphospholipid syndrome (APS), in addition, we analyzed the clinical relations of antibodies to oxLDL in patients with acute coronary syndrome and stable coronary artery disease.

In vitro, we could confirm that high concentrations of oxidized LDL increase proliferation and IL-2, IFN-γ secretion of mononuclear cells in antiphospholipid syndrome. It has been proven that this phenomenon is typical for patients with APS, it can not be observed in lymphocytes separated from healthy individuals. Based on the vascular localization of thromboembolic events, patients with APS were divided into arterious and venous subgroups. The oxLDL stimulus induced Th1-cytokine secretion and lymphocyte proliferation in both subgroups. In consideration of the etiology of venous APS, we suggest that the Th1-derived immune processes can promote persistence of patholological immune responses and worsen the clinical outcome. At the same time, oxLDL triggered Th1-derived immune mechanisms (with dyslipidaemia and anti-β2GPI antibodies) can have an emphasized role in the etiopathogenesis of accelerated atherosclerosis which develops in parallel with arterial thromboses.

It has been detected that the level of IgG-type anti-oxLDL antibodies were elevated both in patients with acute coronary syndrome (ACS) and stable coronary artery disease compared to healthy controls, moreover, these antibodies were present in much larger concentration in acute coronary syndrome. In acute coronary syndrome, it has been confirmed that the elevated initial anti-oxLDL antibody-titer correlate well with unstable clinical events (complications such as circulatory failure, sudden cardiac death, malignant arrhytmias, recurrent angina) during hospitalization. There were significantly lower levels of IgG anti-oxLDL antibodies in patients with ACS on statin therapy compaired to those without statin therapy, which can be due to the pleiotropic (anti-inflammatory) effects of statins. This phenomenon could provide an indirect evidence of close connection between these antibodies and inflammatory processes in the plaque. In ACS, the strong correlation of IgG-type anti-oxLDL antibodies and CRP can also support the important role of these antibodies in the progression of atherosclerotic plaque toward unstability.

In summerizing these results, we conclude that oxidized LDL can stimulate lymphocyte proliferation and secretion of Th1-type cytokines in antiphospholipid syndrome, which results in accelerated atherosclerosis. Moreover, the circulating IgG anti-oxLDL antibodies participate in unstable plaque-associated immune processes and their initial elevation has a predictive value in unstable outcome of acute coronary syndrome.

Keywords: antibodies to oxidized LDL, antiphospholipid syndrome, acute coronary syndrome