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Oxidation of LDL and its clinical implication.

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Abstract

Oxidative modification of low-density lipoprotein (LDL) is one of the earliest events in atherosclerosis. Oxidized LDL (oxLDL) represents a variety of modification of both lipid and apolipoprotein B (apoB) components by lipid peroxidation. This promotes atherosclerosis through inflammatory and immunologic mechanisms that lead to the formation of macrophage foam cells. Recent findings also suggest that oxLDL forms complexes with beta(2)-glycoprotein I (beta(2)GPI) and/or C-reactive protein (CRP) within atherosclerotic lesions and that these complexes appear in the circulation. Autoantibodies (auto-Abs) against oxLDL/beta(2)GPI complexes occur in patients with systemic lupus erythematosus (SLE) and/or antiphospholipid syndrome (APS). These autoantibodies significantly correlate with arterial thrombosis. IgG auto-Abs having similar specificity emerge spontaneously in NZWxBXSB F1 mice, which generally are considered to be an animal model of APS, and these mice produce a monoclonal IgG auto-Ab (WB-CAL-1) against oxLDL/beta(2)GPI complexes. WB-CAL-1 significantly increased the in vitro uptake of oxLDL/beta(2)GPI complexes by macrophages, which suggests that such IgG auto-Abs are pro-atherogenic. In contrast, IgM anti-oxLDL natural Abs found in the atherosclerosis-prone mice have been proposed to be protective. The presence of such Abs in humans has been documented in many publications but their exact pathophysiological significance remains unclear. In this article, we review recent progress in our understanding of the clinical significance of oxidation of LDL, formation of oxLDL complexes, and Abs in atherosclerotic and/or autoimmune disease.

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