BAFF receptor mAb treatment ameliorates development and progression of atherosclerosis in hyperlipidemic ApoE(-/-) mice

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AIMS: Option to attenuate atherosclerosis by depleting B2 cells is currently limited to anti-CD20 antibodies which deplete all B-cell subtypes. In the present study we evaluated the capacity of a monoclonal antibody to B cell activating factor-receptor (BAFFR) to selectively deplete atherogenic B2 cells to prevent both development and progression of atherosclerosis in the ApoE(-/-) mouse. METHODS AND RESULTS: To determine whether the BAFFR antibody prevents atherosclerosis development, we treated ApoE(-/-) mice with the antibody while feeding them a high fat diet (HFD) for 8 weeks. Mature CD93(-) CD19(+) B2 cells were reduced by treatment, spleen B-cell zones disrupted and spleen CD20 mRNA expression decreased while B1a cells and non-B cells were spared. Atherosclerosis was ameliorated in the hyperlipidemic mice and CD19(+) B cells, CD4(+) and CD8(+) T cells were reduced in atherosclerotic lesions. Expressions of proinflammatory cytokines, IL1beta, TNFalpha, and IFNgamma in the lesions were also reduced, while MCP1, MIF and VCAM-1 expressions were unaffected. Plasma immunoglobulins were reduced, but MDA-oxLDL specific antibodies were unaffected. To determine whether anti-BAFFR antibody ameliorates progression of atherosclerosis, we first fed ApoE(-/-) mice a HFD for 6 weeks, and then instigated anti-BAFFR antibody treatment for a further 6 week-HFD. CD93(-) CD19(+) B2 cells were selectively decreased and atherosclerotic lesions were reduced by this treatment. CONCLUSION: Anti-BAFFR monoclonal antibody selectively depletes mature B2 cells while sparing B1a cells, disrupts spleen B-cell zones and ameliorates atherosclerosis development and progression in hyperlipidemic ApoE(-/-) mice. Our findings have potential for clinical translation to manage atherosclerosis-based cardiovascular diseases.
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