**Th1 Immunologic Response in Coronary Microvascular Dysfunction**

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*Background*

 Coronary microvascular dysfunction has been increasingly recognized as the cause for clinical angina in the absence of angiographic evidence of epicardial coronary artery obstruction. Oxidative stress is thought to play a role in microvascular dysfunction via inflammation. The generation of malondialdehyde (MDA) and acetaldehyde (AA) occurs as a result of the lipid peroxidation process and can combine to form a stable protein adduct malondialehyde-acetaldehyde (MAA). Previously anti-MAA antibody isotypes have been associated with the progression and natural history of atherosclerotic disease. The aim of this study was to identify the immune response to oxidative stress mediated biomarkers involved in coronary microvascular dysfunction.

*Methods*

 Patients undergoing cardiac catheterization were evaluated and identified using the comprehensive diagnostic algorithm to identify the presence of coronary microvascular dysfunction. Subjects were consented through IRB into the Nebraska Cardiovascular Biobank (NCBR) for blood and clinical parameter collection for research. Inclusion and exclusion criteria were primarily focused on coronary flow measurements – Coronary flow reserve (CFR) and fractional flow reserve (FFR). Blood samples were taken at the time of catheterization and tested for the following biomarkers: anti-MAA antibody isotype ELISA testing, thiobarbituric acid reactive substance (TBARS) assay, asymmetrical dimethylarginine (ADMA) assay, ProBNP assay, and multiplex immunoassay to identify a number of specific adaptive immunological profiles.

*Results*

 Comparison of the microvascular disease population with normal coronary flow reserve samples showed anti-MAA antibody isotype switching occurs, resulting in an elevated IgG (p<0.03) and IgA (p<0.05) level in the microvascular disease population. Elevation of asymmetrical dimethylarginine (p<0.01) and endothelin-1 (p<0.01) suggested endothelial dysfunction. In addition, there is elevation in the inflammatory markers urokinase-type plasminogen activator receptor (p<0.05) and serpin E1 (p<0.02). Cytokines, interleukin-2 (p<0.02) and interleukin-12 (p<0.04) were significantly elevated in the microvascular dysfunction group.

*Conclusions*

 This study demonstrated an increase in oxidative stress increased IgG and IgA anti-MAA antibody levels in patients with microvascular disease. The role of endothelial dysfunction is corroborated by the elevation of ADMA and endothlin-1. Also, an increase in the cytokines IL-2 and IL-12 suggests a Th1 immune response and perpetuating the inflammatory cascade in coronary microvascular dysfunction.