1493 - Atherosclerosis Biomarkers in Systemic Sclerosis- A Multiplex Analysis

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Hall F2 - Poster Hall (McCormick Place West)

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Background/Purpose: Increasing evidence suggests that atherosclerosis is increased in systemic sclerosis (SSc) compared to healthy individuals. However, the pathogenesis of atherosclerosis in SSc remains unknown. This study aimed to identify markers of fibrosis, vasculopathy, and inflammation that may be involved in the pathogenesis of atherosclerosis in a female SSc cohort.

Method: The multiplex antibody array, based upon enzyme-linked immunosorbent assay (ELISA) technology, can measure multiple proteins simultaneously within a single sample. We utilized a microplate-based multiplex platform (Aushon Biosystems SearchLight) to identify 100 proteins in plasma samples from females with SSc with no history of atherosclerosis (N=46). In addition, circulating type I Interferon (IFN) activity was quantified by exposing epithelial cells to SSc serum and quantifying IFN-inducible genes by real-time PCR. All subjects underwent bilateral carotid ultrasounds to quantify plaque and intima-medial thickness (IMT) and were read by a single reader (NR). Statistical analysis was performed using Wilcoxin rank-sum test and Spearman's correlation. Significance was determined at $P<0.05$; no statistical adjustment was performed for multiple-testing as this analysis was hypothesis generating.

Result: Mean age (+/- SD) of the subjects was 48.6 (+/- 13.3) years. Carotid plaque was detected in 21 (46%) of the SSc subjects. Multiplex analysis detected significant associations between biomarkers of inflammation, vasculopathy, and fibrosis with atherosclerosis in the SSc subjects. IL-2, IL-6, CRP, KGF, ICAM-1, endoglin, PAI-1, and IGFBP3 were associated with carotid plaque ($P<0.05$, Table 1). MPIF1, A-SAA, thrombomodulin, NTpBNP, and CC16 were correlated with carotid IMT ($P<0.5$, Table 2). Type I IFN signatures were not associated with plaque or CIMT in SSc.

Table 1: Proteins associated with carotid plaque in SSc

	BIOMARKER (pg/ml)	NO PLAQUE, mean(SD)	PLAQUE, mean(SD)	*P*-value
Inflammation	IL-2	3.0 (2.6)	5.0 (3.8)	0.03
	IL-6	11.0 (13.5)	25.2 (48.5)	0.05
	CRP	1627772 (2437838.6)	3856899.5 (4734651.2)	0.01
Vasculopathy	KGF	0.8 (2.1)	1.6 (2.1)	0.02
	ICAM-1	403423.3 (131159.9)	539301.8 (242768.3)	0.04
	Endoglin	22444.1 (9253)	28156.3 (8860.8)	0.04
Fibrosis	PAI-1	9607.8 (6527.1)	6680 (5898)	0.05
	IGFBP3	404848.8 (116838.8)	322117.3 (93709)	0.01

Table 2: Correlation of proteins with carotid IMT in SSc

	BIOMARKER	IMT (r)	*P*-value
Inflammation	MPIF-1	0.31	0.04
	A-SAA	0.31	0.04
Vasculopathy	Thrombomodulin	0.32	0.04
	NTpBNP	0.42	0.01
Fibrosis	CC16	0.37	0.01

Conclusion: Distinct biomarkers of inflammation, vasculopathy, and fibrosis are associated with carotid plaque and IMT in SSc. Factors associated with carotid IMT differ from those associated with plaque in SSc. Further studies are needed to confirm the validity of these associations in another SSc cohort and their putative role as biomarkers of vascular events in this disease.

Keywords: atherosclerosis, biomarkers, scleroderma and systemic sclerosis

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