T-Cell Activation and E-Selectin Associated with Coronary Plaque in HIV-Infected Youth

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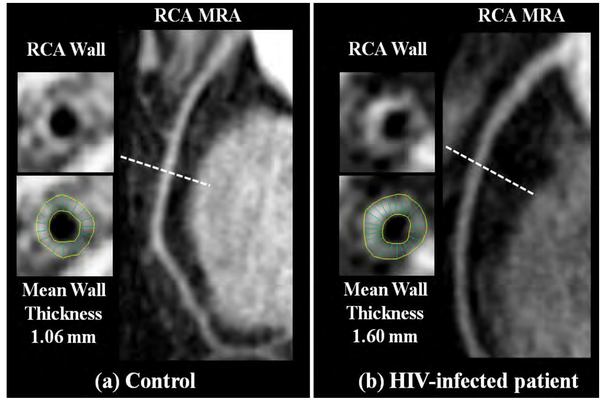
BACKGROUND

- Young adults infected with HIV early in life may be at increased risk for premature coronary artery disease (CAD)
- Research in adults with HIV indicates that chronic immune activation may play a role in coronary plaque formation
- Measuring immune markers and biomarkers of vascular dysfunction may provide insight to the atherogenic process in this population
- Early signs of cardiac and vascular dysfunction in asymptomatic young adults with life-long HIV infection and healthy controls were compared using CT angiography and black-blood coronary vessel wall imaging by MRI

METHODS

- Prospective cross-sectional study of 35 youth and young adults who acquired HIV in early life and 11 sex and race matched healthy controls, all free of active CVD
- Phase-sensitive dual inversion recovery black-blood vessel wall imaging was utilized for MR imaging of the proximal right coronary artery (RCA)
- CT angiography was performed for determination of coronary plaque burden. Coronary plaque burden was scored based on a standardized scale for number, severity, and luminal narrowing.
- Nadir CD4 and lifetime ART exposure were characterized by review of clinical history
- Fasting laboratories included chemistry, lipid panel, CD4 T cell counts, HIV viral load, biomarkers of inflammation and vascular injury, and immune markers.
- Nonparametric Wilcoxon rank-sum tests were performed. Values in data tables are presented as mean ± SD unless otherwise indicated.

Figure 1: Phase-sensitive dual inversion-recovery (PS-DIR) black-blood vessel MR imaging of the proximal right coronary artery (RCA) in (a) a control subject and (b) an HIV-infected patient



RESULTS

Table 1: Demographic and clinical characteristics, including CT and MRI measurements, of participants.

	HIV+ (n=35)	Control (n=11)	P-value
Age, years	22 ± 4	25 ± 2	**0.007**
Sex: Male/Female (%)	54/46	27/73	0.12
BMI (kg/m^2)	23.9 ± 5.7	26.1 ± 4.8	**0.047**
Ever Smoked, n (%)	10 (29)	2 (18)	0.48
Smoking Pack years	0.8 ± 2.2	0.07 ± 0.2	0.36
Systolic BP (mmHg)	123 ± 14	116 ± 6	**0.04**
Diastolic BP (mmHg)	73 ± 8	67 ± 7	**0.03**
Hypertension, n (%)	4 (11)	0 (0)	0.13
Total Cholesterol (mg/dL)	152 ± 31	177 ± 28	**0.02**
LDL (mg/dL)	89 ± 34	98 ±26	0.14
HDL (mg/dL)	47 ± 12	65 ± 12	**0.0002**
hs-CRP (mg/mL)	3.2 ± 5.3	1.7 ±1.4	0.88
Current CD4 (cells/μL)	502 ± 306	781 ± 184	**0.008**
Hx of Lipid Rx, n (%)	1 (3)	0 (0)	0.3
Framingham Risk (%)	0.01 ± 0.05	0	0.6
Number of coronary plaque lesions	0.3 ± 0.8	1.3 ± 2.2	0.08
Size of coronary plaque score	0.4 ± 1.2	1.3 ± 2.2	0.09
Severity of luminal narrowing score	0.5 ± 1.9	1.4 ± 2.5	0.09
RCA vessel wall thickness (mm)	1.32 ± 0.21	1.09 ± 0.14	**0.002**

Table 2: Clinical characteristics of the HIV+ group.

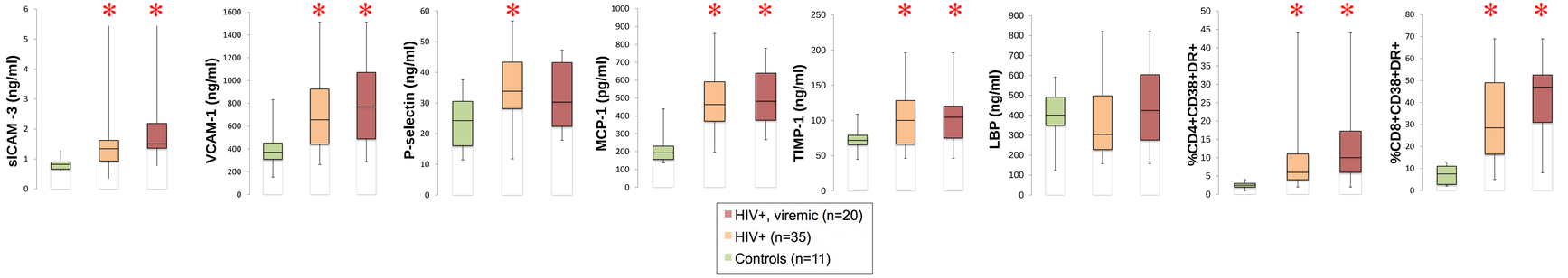
	HIV+ (n=35)
Current ARV use, n (%)	25 (71)
Duration ARV use, years	15 ± 5
Duration Protease Inhibitors, years	9 ± 5
Duration Nucleoside Reverse Transcriptase Inhibitors, years	15 ± 5
Duration Non-nucleoside Reverse Transcriptase Inhibitors, years	4 ± 4
CD4 < 200 (cells/μL), n (%)	5 (14)
Nadir CD4 (cells/μL)	202 ± 186
HIV RNA <50 copies/mL, n (%)	15 (43)

Table 3: Correlation of clinical characteristics and biomarkers to coronary artery plaque among HIV-infected subjects.

	Correlation Coefficient	P-value	Model 1		Model 2	
			Estimate	P-value	Estimate	P-value
Age (y)	0.002	0.99	0.04	0.08	0.04	0.07
Smoking pack-years (y)	0.08	0.7	0.08	0.77	-0.008	0.76
E-selectin (ng/mL)	0.48	**0.006**	0.005	0.76	0.003	0.84
Current CD8+CD38+DR+ (%)	0.46	**0.025**	0.012	**0.01**	0.0097	**0.04**
LDL Cholesterol (mg/dL)	0.78	**< 0.001**	--	--	0.002	0.51

Model 1 is a multivariate regression analysis including age, smoking pack-years, E-selectin, and CD8+CD38+DR+. Model 2 is a multivariate regression analysis including age, smoking pack-years, E-selectin, CD8+CD38+DR+, and LDL.

Figure 2: Box plot of levels of biomarkers of vascular dysfunction of control subjects vs. all HIV-infected patients and in the subset of HIV-infected patients with a viral load of >50 copies/mL. Box plots are displayed as median and IQR. * indicated for p-values < 0.05 compared to controls.



CONCLUSIONS

- Individuals infected with HIV early in life have higher levels of immune activation, inflammation, and circulating adhesion molecules than controls
- Viral suppression of HIV helps reduce but not completely reverse the chronic inflammatory state of HIV
- Immune activation, in particular %CD8+CD38+DR+, is associated with coronary plaque in this cohort of patients with HIV