ROLE OF ANGIOPOETIN-1, ANGIOPOETIN-2, AND ENDOTHELIAL FUNCTION IN HIV

Poster Contributions
Poster Hall B1
Monday, March 16, 2015, 9:45 a.m.-10:30 a.m.

Session Title: Vascular Medicine Potpourri
Abstract Category: 43. Vascular Medicine: Basic
Presentation Number: 1259-335

Authors: Mark Joshua Dela Cruz, Y. Ma, Rebecca Scherzer, Alan Wu, Kristinalisa Maka, Steven Deeks, Peter Ganz, Priscilla Hsue, University of California, San Francisco, San Francisco, CA, USA

Background: HIV-infected patients have increased risk for cardiovascular disease (CVD). The underlying mechanism likely involves endothelial dysfunction, a precursor of atherosclerosis. Endothelial homeostasis is promoted by the Tie2 receptor system through its agonist, angiopoietin-1 (Ang1) while its antagonist, the inflammatory protein angiopoietin-2 (Ang2), promotes endothelial activation. We hypothesized that HIV infection is associated with decreased Ang1 and increased Ang2 levels, leading to impaired endothelial function.

Methods: We performed a cross-sectional analysis of Ang1 and Ang2 serum levels by ELISA, among 89 HIV-infected subjects, and 46 uninfected controls. Endothelial function was measured by flow-mediated dilation of the brachial artery (FMD). Generalized linear regression models were used to determine the association of HIV to Ang1/Ang2 levels and FMD.

Results: The median age was 49 yrs and 87% were male. Compared to controls, HIV subjects were younger (median age 45 vs 53 yrs, p=0.03), less likely to be male (82% vs 98%, p=0.03), and more likely to have renal disease (eGFR<60) (13.5% vs 2.2%, p=0.04). Forty-seven (53%) HIV subjects were effectively treated. Compared to controls, Ang1 levels were lower in HIV subjects (median 2,219 pg/ml, IQR 1,022 to 4,280, p= 0.01) while Ang2 levels were higher (median 2,147 pg/ml, IQR 1,617 to 3,106, p=0.06). After adjustment for traditional risk factors, Ang1 levels remained lower in HIV subjects compared to controls (-43.8%, p=0.018) but Ang2 levels were no longer different (p=0.65). Individuals on effective ART had 29% lower Ang1 levels compared to controls in adjusted analysis (p=0.01) and lower Ang1 levels were independently associated with impaired FMD (p<0.001).

Conclusion: Circulating Ang1 levels are reduced among HIV-infected subjects compared to controls, even in those on effective ART. Lower Ang1 is independently associated with impaired endothelial function. These data suggest that HIV infection leads to an imbalance between Ang1 and Ang2, resulting in endothelial dysfunction through the Tie2 receptor system. Our findings reveal a potential new target for mitigating CVD risk in the setting of treated HIV infection.