The Contribution of Hiv to Brain Arterial Remodeling: A Case-control Study

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Background: The incidence of cerebrovascular events is rising in the HIV population but little is known about the mechanisms of vascular injury among patients with HIV population.

Methods: Large cerebral arteries were obtained from autopsies in 80 HIV+ cases and 80 HIV- controls, matched for sex and age ± 3 years, range 30-84. Arterial size, atherosclerosis phenotype, luminal stenosis, and media thickness were obtained in each artery. The average pixel intensities (AI) of metalloproteinase (MMP)-2, MMP-3, MMP-9, tissue inhibitor of MMP (TIMP)-1 and TIMP-2 was assessed with immunohistochemistry defining high intensity as an AI in the upper tertile. Inflammation was assessed with CD68 staining. All estimates were adjusted for age, sex, ethnicity, vascular risk factors and cocaine use.

Results: Arterial inflammation was associated with greater staining intensity of MMP3 (Beta=0.36, P=0.003) and TIMP2 (Beta=0.29, P=0.002) in HIV+ cases, but not in HIV- controls. The association of HIV with MMP3 was independent of whether the inflammation was located in the media, intima, or adventitia, while for TIMP-2 the association was only significant with intima inflammation (Beta=-0.36, P=0.03). Cerebral arteries in HIV+ cases with high intensity of MMP3 staining had thinner media (Beta=-2.3, P= 50 viral copies/mL (B=0.62, P=0.04), Nucleoside Reverse Transcriptase Inhibitor (B=1.08, P=0.009) or protease inhibitor use at the time of death (B=-0.64, P=0.05), vascular risk factors (B=0.51, P=<0.001), and diabetes (B=1.2, P=<0.001), were associated with higher expression of MMP3. There were no significant associations between inflammation and MMP2, MMP9 and TIMP1 intensity staining.

Conclusions: Arterial inflammation in HIV+ cases is associated with greater expression of MMP3, and arteries with higher expression of MMP3 have a thinner media, despite thicker walls, and greater degrees of luminal narrowing. Through thinning of the media, MMP3 may play a role in HIV-associated dolichoectasia; through secondary effects, it may contribute to paradoxical luminal stenosis.