1111-132 Unique Coronary Arteriopathy Associated With Human Immunodeficiency Virus

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Background: The human immunodeficiency virus (HIV) is associated with vascular endothelium abnormalities including increased leukocyte adhesion and increased endothelium turnover. The HIV population also has an increased incidence of peripheral atherosclerosis. This study was designed to characterize the pathologic features of coronary arteries associated with HIV.

Methods: We reviewed all Mayo Clinic autopsies performed on adult subjects ≤60 years with HIV. The study included 32 male patients (mean 41 years; range, 23–60 years) with late stage HIV disease and 32 age-matched controls. An independent observer examined the left anterior descending coronary artery under light microscopy for abnormalities in the vessel wall and the grade of coronary atherosclerosis (CAD).

Results: There were no differences in cardiovascular risk factors or the incidence or grade of CAD between the groups.

	% CAD (mean grade)	Intimal Elastosis	Medial Dysplasia
HIV+	50.0% (1.7 ± 1.0)	50.0%[*]	40.0%[*]
Controls	65.6% (1.4 ± 1.2)	6.3%	15.0%

[*]p ≤ 0.05

However, there were differences in the structure of the intima and media.

Conclusion: Despite an equal incidence of coronary atherosclerosis, HIV is associated with unique histologic findings. This may suggest an involvement of the coronary arteries in HIV disease.

1111-133 Chlamydia and HLA-DR Genotypes in Coronary Atherosclerosis

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To investigate the role of Chlamydia pneumoniae in the pathogenesis in coronary atherosclerosis, presence of Chlamydia was determined post-mortem in 60 subjects with CAD. Atherosclerosis was graded microscopically in a blinded fashion by two investigators and classified as severe or mild based on intimal-medial thickening. Multiple sections of coronary arteries were examined for Chlamydia by immunohistochemistry using a specific monoclonal antibody. Serum was used for measurement of total and HDL-cholesterol and lipoprotein (a) levels. HLA-DR genotypes were determined in cardiac muscle. Thirty six of 42 regions with severe atherosclerosis were immunopositive for Chlamydia compared to 1 of 18 with mild atherosclerosis (p < 0.001). Serum total and HDL-cholesterol levels were similar in both groups, but mean lipoprotein (a) levels were higher in cases with severe atherosclerosis (199 ± 44 vs 61 ± 12 mg/L in cases with mild atherosclerosis, p < 0.04). Nine cases had lipoprotein (a) levels >200 mg/L; all these had severe atherosclerosis. Seventeen of 35 cases with severe atherosclerosis were positive for HLA-DR 13 or 17 as compared to 3 of 15 cases with slight atherosclerosis (p < 0.01). In a substudy, 16 adjacent section 1 from coronary arteries were studied by both PCR and immunohistochemistry. The results failed to show a significant correlation between the two methods. This study shows a positive correlation between presence of Chlamydia and severity of coronary atherosclerosis. This study also supports the hypothesis that atherosclerosis is an autoimmune process triggered by an intracellular infection in subjects with high lipoprotein (a) levels and certain inherited HLA-DR genotypes (13 and 17).

1111-134 Monocytes of Patients With Recurrent Unstable Angina Are Hyper-Responsive to Lypopolysaccharide Challenge

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Background: Raised levels of C-reactive protein (CRP) have been associated with short- and long-term occurrence of coronary events. To investigate whether raised levels of CRP in unstable angina (UA) are related to an enhanced cytokine production in response to inflammatory stimuli we studied 26 pts with history of UA, followed for 22 ± 10 months, who were free of symptoms from >6 months (G1); we also studied 12 pts with chronic stable angina (G2) and 14 healthy subjects (G3).

Methods: G1 pts were subgrouped according to CRP levels at the study time: G1a consisted of 14 pts with CRP levels >3 mg/l and G1b of 12 pts with CRP <3 mg/l. CRP was normal in all G2 and G3 subjects. 10/14 G1a pts had coronary events during the follow-up. In contrast, no G1b of 12 pts had new coronary events (P < 0.001).

In all groups we assessed the interleukin-6 (IL-6) production by peripheral blood mononuclear cells after stimulation of 1 ml of whole blood with 1 ng of lypopolysaccharide (LPS) for 4 hours.

Results: At baseline LPS-stimulated production of IL-6 was significantly higher in G1a (median 4264 pg/ml) than in G1b (1752 pg/ml), G2 (707 pg/ml) and G3 (488 pg/ml) (all P < 0.001). No significant differences were observed among G1b, G2, G3. No differences were found in monocyte and lymphocyte count among the 4 groups.

Conclusion: Persistently elevated levels of CRP after hospital discharge in UA represent a marker of inflammatory cell hyper-responsiveness, associated with the recurrence of coronary events, which may be related to monocyte hyper-response to inflammatory stimuli.

1111-135 Abnormal Coronary Vasomotor Response to Mental Stress in Patients With Coronary Artery Disease (CAD)

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Background: Mental stress (MS) provokes symptomatic or silent myocardial ischemia in patients with CAD. However, little is known regarding the underlying pathophysiological mechanisms of MS-induced ischemia.

Methods and Results: We therefore investigated the hemodynamic, neurohumoral and myocardial blood flow (MBF) responses to MS in 15 patients (pts.) with CAD (9 m/6 f, mean age: 62 ± 11 years) and 23 healthy controls (14 m/9 f, mean age: 48 ± 12 years). MS was induced by asking individuals to solve mathematical subtractions in a progressively challenging sequence. The rate pressure product (RPP) as index of cardiac work was calculated at 1 min intervals and MBF was quantified at rest and during MS using ^{13}N-ammonia - PET imaging. The RPP increased in controls from 8402 ± 2331 to 10456 ± 2775 and in pts. from 7836 ± 1880 to 10605 ± 3044 and (p = NS vs. controls). Increases in serum norepinephrine (20 vs. 20%) and epinephrine (45 vs. 35%; p = NS) were also similar in both groups. In controls, MS induced proportional increases in MBF (0.69 ± 0.16 vs 0.95 ± 0.23 ml/g/min) and cardiac work (r = 0.7; p < 0.01) while no such relationship was observed in pts. Consequently, MBF normalized to the RPP remained unchanged in controls (0.89 ± 0.18 vs. 0.90 ± 0.14; p = NS) but declined from 1.00 ± 0.25 to 0.85 ± 0.23 in pts. (p < 0.01). The coronary resistance declined from 137 ± 29 to 114 ± 16 ml/min/g/mmHg in controls but remained unchanged in pts. Discriminant and logistic regression analysis revealed normalized MBF response to MS as the only variable differentiating between pts. and controls, and presence of CAD was the strongest predictor for an abnormal MBF response to MS.

Conclusion: MS detects abnormalities in coronary vasomotion in pts with CAD which might explain their susceptibility to ischemic events during stressful daily life events.

1111-136 Eosinophil Counts Correlate With Fibrinogen Levels in Patients With Vasospastic Angina

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Background: Epidemiologic studies suggested a relationship between white blood cell counts (WBC) and the incidence of coronary heart disease. Vasospastic angina (VSA) is caused by coronary spasm, however, the mechanism of coronary spasm remains to be elucidated.

Method: To clarify the relation of WBC and differential in VSA, we compared hematologic values, blood chemical values, fibrinogen, C-reactive protein, and coronary risk factors in VSA patients (pts) with those in stable effort angina pectoris pts (sAP, n = 32) and control subjects (C, n = 10). VSA pts were further divided into mild (m)-VSA (n = 16) and severe (s)-VSA groups (n = 16) according to the severity of the symptoms.

Results: There were no differences in coronary risk factors, body temperature, WBC, C-reactive protein among groups, however, eosinophil counts were significantly higher in s-VSA than other three groups (C = 173 ± 141/mm^3, sAP = 141 ± 78, m-VSA = 185 ± 66, s-VSA = 305 ± 97; p < 0.01). Fibrinogen levels were also significantly higher in s-VSA than other three groups (C = 287 ± 66 mg/dl, sAP = 291 ± 49, m-VSA = 306 ± 77, s-VSA = 403 ± 94; p < 0.05). Only eosinophil counts in WBC and differential positively correlated with fibrinogen levels in the study subjects (r = 0.432; p < 0.01). Follow-up study of VSA (n = 20) demonstrated that, after medication, eosinophil counts in VSA significantly decreased to the same level as C (before medication; 265 ± 94 vs after medication; 143 ± 90; p < 0.001).

Conclusions: Thus, eosinophil counts and fibrinogen levels may be determinant factors for the severity of VSA and play an important role in the pathogenesis of VSA. Furthermore, follow-up study suggests that coronary spasm might result in the increase in eosinophil counts and fibrinogen levels in VSA.