Cardiac Allograft Vascular Disease. Relationship to microvascular cell surface markers and inflammatory cell phenotypes on endomyocardial biopsy

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Abstract

Background

Cardiac allograft vascular disease is characterized by accelerated and diffuse intimal proliferation involving both the microvasculature and epicardial vessels. Because in vivo documentation of this complication is now possible with intracoronary ultrasound imaging, we can examine the relationship of intimal proliferation to markers of immunity and endothelial activation. We hypothesize that alterations of microvascular cell surface markers likely mirror changes in the epicardial vessels that may be important in the pathophysiology of intimal proliferation.

Methods and Results

Forty-three heart transplant patients were examined by intracoronary ultrasound more than 1 year after transplantation, and these images were analyzed to obtain mean intimal thickness and intimal thickness class (I through IV), calculated from the mean thickness and circumferential involvement. Right ventricular endomyocardial biopsies obtained at the time of intracoronary ultrasound were examined by immunohistochemistry to detect microvascular expression of histocompatibility leukocyte antigen (HLA) classes I and II (HLA ABC, DR, DP, and DQ); endothelial-specific antigen detected by the monoclonal antibody E 1.5; intercellular adhesion molecules (ICAM-1); CD4+ and CD8+ lymphocytes and macrophages (CD 14+). Microvascular antigen expression was graded 1 through 5 on the basis of the diffuseness of positive staining. The number of each inflammatory cell phenotype present per high-power field was counted. By ANOVA, scores for HLA DR, HLA DQ, and E1.5 expression were lower in intimal thickness classes II, III, and IV compared with class I. This inverse relationship was significant by linear regression analysis of mean intimal thickness. Inflammatory cells were not significantly correlated with intimal thickening. Rejection incidence was higher, and time since transplantation longer, in intimal thickness classes II, III, and IV compared with class I.

Conclusion

Transplant coronary artery intimal proliferation is associated with alteration of microvascular endothelial cell surface markers. These changes in cell surface antigen expression could provide the substrate for coronary artery intimal proliferation and narrowing.

Keywords

Antigens, transplantation, endothelium