Immunologic basis of transplant-associated arteriosclerosis.

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Abstract

Although immunosuppressive therapy minimizes the risk of graft failure due to acute rejection, transplant-associated arteriosclerosis of the coronary arteries remains a significant obstacle to the long-term survival of heart transplant recipients. The participation of specific inflammatory cell types in the genesis of this lesion was examined in a mouse model in which carotid arteries were transplanted across multiple histocompatibility barriers into seven mutant strains with immunologic defects. An acquired immune response--with the participation of CD4+ (helper) T cells, humoral antibody, and macrophages--was essential to the development of the concentric neointimal proliferation and luminal narrowing characteristic of transplant arteriosclerosis. CD8+ (cytotoxic) T cells and natural killer cells were not involved in the process. Arteries allografted into mice deficient in both T-cell receptors and humoral antibody showed almost no neointimal proliferation, whereas those grafted into mice deficient only in helper T cells, humoral antibody, or macrophages developed small neointimas. These small neointimas and the large neointimas of arteries grafted into control animals contained a similar number of inflammatory cells; however, smooth muscle cell number and collagen deposition were diminished in the small neointimas. Also, the degree of inflammatory reaction in the adventitia did not correlate with the size of the neointima. Thus, the reduction in neointimal size in arteries allografted into mice deficient in helper T cells, humoral antibody, or macrophages may be accounted for by a decrease in smooth muscle cell migration or proliferation.