***Vascular dendritic cells* express intercellular adhesion molecule-1 in atherosclerotic plaques**

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ABSTRACT

The presence of activated T cells in human atherosclerotic lesions is well established and cell adhesion molecules are thought to be regulators of T cell activation. Since the critical role of antigen-presenting *dendritic cells* in T cell activation with ICAM-1/LFA-1 is now recognized, we wondered whether CD1a⁺ *vascular dendritic cells* express ICAM-1 in atherosclerotic lesions. Immunohistochemical analysis demonstrated that CD1a⁺ *vascular dendritic cells* mostly reside within inflammatory infiltrates located near neovascularization sites and that CD1a⁺ cells express ICAM-1. These observations support an opinion that *vascular dendritic cells* might be involved in immune mechanisms in atherogenesis.

Atherosclerotic plaques are characterized by inflammatory infiltrates consisting of macrophages and activated T cells, although how cellular activation occurs remains undefined. Adhesive molecules involved in direct T cell interactions are critical to T cell activation, and recent studies demonstrated that ICAM-1 which is a 'counter receptor' for the lymphocyte activation antigen (LFA-1), is expressed in human atherosclerotic lesions (7, 9, 10). ICAM-1 is expressed by endothelial cells, smooth muscle cells, and macrophages as well as by unidentified cells that do not mark with cell-type specific antibodies such as HHF35 (smooth muscle cells), HAM 56 (macrophages) or antibodies to CD45 (lymphocytes) or factor VIII related antigen (endothelium). In some quantitative studies the subset of 10F3 positive (ICAM-1⁺) nonidentified cells amounted to about half of the antigen presenting cells (9).

We recently demonstrated that antigen presenting *dendritic cells* are involved in atherogenesis (1–5) and we expected that ICAM-1⁺ 'null' cells (9) might be *vascular dendritic cells*.

Vascular dendritic cells in the arterial intima strongly express HLA-DR (5), stain positively for

S-100 (1–5) and exhibit ultrastructural features typical of other *dendritic cells* including a distinctive tubulovesicular apparatus (1, 4, 5). *Vascular dendritic cells* do not express CD68, CD3 or smooth muscle alpha-actin but display a highly specific antigen of *Langerhans cells*-CD1a (1, 3–5) which allows them to be identified unambiguously. Mature *vascular dendritic cells* are rare in nonatherosclerotic intima but are common in atherosclerotic lesions where they often locate amongst CD3⁺ and CD68⁺ cells in inflammatory infiltrates (4, 5). Direct contacts between *vascular dendritic cells* and T lymphocyte-like cells have also been detected in an electron microscopic examination (1).

To verify our speculation that *vascular dendritic cells* might express ICAM-1, we analyzed consecutive arterial frozen sections stained with either anti-CD1a (DAKO-CD1a, clone NA1/34, dilution 1:50) or anti-ICAM-1 (Immunotech, CD54-ICAM-1, clone 84H10; dilution 1:50) using ABC immunoperoxidase technique as previously (1–5). All the specimens of carotid arteries (n = 17) and aortas (n = 12) contained ICAM-1⁺ cells with ICAM-1 immunoreactivity irregularly distributed through plaques with ICAM-1 expression most intensively associated with the zones of neovascularization. The CD1a⁺ cells with a dendritic appearance were distributed throughout the athero-

Fig. 1 CD1a⁺ cells located in a neovascularization area containing an inflammatory infiltrate. Human aorta. ABC immunoperoxidase technique, counterstaining with Mayer's hematoxylin. $\times 400$

sclerotic intima but they were more frequent near the neovasculature and within inflammatory infiltrates (Fig. 1). The patterns of CD1a⁺ cell distribution were consistent with our previous observations (4, 5). During examination of the plaque areas where the populating cells were frequently intermingled and closely apposed, we failed to identify the same cells in parallel adjacent sections and so, we could not determine which cell types displayed ICAM-1. However, some intimal loci consisted mostly of CD1a⁺ cells and analysis of the adjacent sections confirmed that these cells were also ICAM-1 positive (Fig. 2).

These observations imply that the behavior of *vascular dendritic cells* is similar to that of other T cell associated *dendritic cells* expressing high levels of ICAM-1 (6). The ICAM-1/LFA-1 interactions appear to be important in *dendritic cell*/T cell interactions (6) and a similar mechanism might be true in atherogenesis. Since *dendritic cells* are the most potent accessory cells known to activate T lymphocyte responses (6), we speculate that *vascular dendritic cells* may mediate a local immune response in atherosclerotic lesions. Co-expression of ICAM-1 and CD1a on the surface of *vascular dendritic cells* might be significant as it seems that

CD1 is an antigen-presenting molecule in the same sense as the classical MHC class I and II molecules (8). Although MHC-restricted T cells predominate in most immune responses, CD1-restricted responses may be important in atherosclerosis.

We thank St. Vincent's Clinic Foundation for financial support.

Received 27 November 1996; and accepted 20 December 1996

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Fig. 2 CD1a⁺ cells (a, c)/ICAM-1⁺ cells (b, d) (arrows) in an atherosclerotic plaque of the human aorta (parallel sections). c, detail of a; d, detail of b. ABC immunoperoxidase technique, counterstaining with Mayer's hematoxylin. a and b, $\times 100$; c and d, $\times 400$

Fig. 2

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