LOW EXPRESSION OF E-SELECTIN IN DISEASED TISSUES FROM HUMAN IMMUNODEFICIENCY VIRUS-POSITIVE PATIENTS

To the Editor:

In the November 1, 1993 issue of Blood, Hofman et al reported an in vitro study showing that tat protein of human immunodeficiency virus (HIV) activates human umbilical vein endothelial cell cultures to express E-selectin and suggested that through this mechanism, tat has a relevant role in the extravascular dissemination of HIV.

We have recently investigated endothelial cell activation in pathologic tissues from HIV+ and HIV- patients, using immunocytochemistry. Expression of ICAM-1, E-selectin, and VCAM-1 was evaluated in 15 lymph nodes of HIV+ patients affected by persistent generalized lymphadenopathy (PGL) and in 18 reactive lymph nodes of HIV+ patients (Table 1). Immunostaining for E-selectin was detected in a few paracortical high endothelial venules (HEVs) in 3/14 HIV+ lymph nodes and in 6/18 HIV+ lymph nodes. A marked reactivity for ICAM-1 was present in most HEVs of all investigated cases. Blood vessels were consistently negative for VCAM-1 in both groups.

It has been suggested that macrophages are tissue reservoirs of the virus, particularly in the central nervous system in acquired immune deficiency syndrome dementia. We have investigated the expression of E-selectin, ICAM-1, and VCAM-1 in blood vessels of autopsic brain tissue obtained from 7 HIV+ and 10 HIV- patients (Table 2). In HIV+ patients, two brain samples were histologically normal, two were involved by HIV-related microglial nodule encephalitis, and three by JC virus-associated progressive multifocal leukoencephalopathy (PML). Vascular endothelium was reactive for ICAM-1 in normal and pathologic brain tissue. In PML, staining for E-selectin and VCAM-1 was detected only in those blood vessels associated with prominent perivascular lymphocyte infiltrates and with intense macrophage reaction. In the two cases of HIV-related encephalitis, blood vessels were negative for E-selectin and VCAM-1.

In conclusion, our findings do not show an extensive or increased expression of E-selectin in the endothelium of pathologic tissues from HIV+ patients. Obviously, the possibility that tat-induced expression of E-selectin has a relevant pathogenetic role in the early phases of HIV infection cannot be ruled out.

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RESPONSE

In our recent report in Blood, we provided evidence that the tat protein upregulates the expression of the endothelial cell adhesion molecule, E-selectin. As has been extensively reported, the expression of this molecule is upregulated within 3 to 4 hours of endothelial cell activation and returns to baseline values by 24 to 48 hours. In the letter by Uccine et al, they presented data showing that in human immunodeficiency virus+ brain samples as well as HIV+ lymph node tissue show no significant increased expression of E-selectin and VCAM-1 above normal HIV+ tissue samples. Our experience with HIV(+) central nervous system (CNS) tissues is quite different. We have examined brain samples from HIV+ AIDS patients with no apparent encephalitis, with detectable encephalitis, and with opportunistic CNS infection, for E-selectin and VCAM-1 expression. Using immunocytochemistry with the avidin-biotin peroxidase procedure
and monoclonal antibodies to E-selectin and VCAM-1 (AMAC Inc, Westbrooke, ME), we observed staining for E-selectin and VCAM-1 in the white matter of cryostat sections. These adhesion molecules were expressed on both blood vessels associated with perivascular infiltrates and those with no apparent perivascular infiltrates. The brain with CNS opportunistic infection showed the most dramatic upregulation of both these adhesion molecules. In the AIDS patients with and without HIV encephalitis, VCAM-1 was intensely expressed, whereas E-selectin was faint but focally present. Normal HIV brain tissue was negative. Others have shown that in simian immunodeficiency virus, VCAM-1 was abundantly expressed on vascular cells in the brain, although E-selectin was focally detected in only a limited number of animals.1

These data suggest that both E-selectin and VCAM-1 are present in AIDS encephalitis. VCAM-1 does appear to be more intense and wide spread compared with E-selectin. Perhaps the lower expression of E-selectin may be a reflection of the transitory nature of this molecule. However, because these adhesion markers are present, molecules that regulate E-selectin and VCAM-1 or their ligands are likely to be important in AIDS.

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Low expression of E-selectin in diseased tissues from human immunodeficiency virus-positive patients [letter; comment]

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