Fimbria-dependent activation of cell adhesion molecule expression in Porphyromonas gingivalis-infected endothelial cells.

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Abstract

Porphyromonas gingivalis is an oral pathogen that has recently been associated with chronic inflammatory diseases such as atherosclerosis. The strength of the epidemiological associations of P. gingivalis with atherosclerosis can be increased by the demonstration that P. gingivalis can initiate and sustain growth in human vascular cells. We previously established that P. gingivalis can invade aortic, heart, and human umbilical vein endothelial cells (HUVEC), that fimbriae are required for invasion of endothelial cells, and that fimbrillin peptides can induce the expression of the chemokines interleukin 8 and monocyte chemotactic protein. In this study, we examined the expression of surface-associated cell adhesion molecules on endothelial cells in response to P. gingivalis infection by fluorescence-activated cell sorting FACS analysis and confocal microscopy. Coculture of HUVEC with P. gingivalis strain 381 or A7436 resulted in the induction in the expression of intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1) and P- and E-selectins, which was maximal at 48 h postinfection. In contrast, we did not observe induction of ICAM-1, VCAM-1, or P- or E-selectin expression in HUVEC cultured with the noninvasive P. gingivalis fimA mutant DPG3 or when P. gingivalis was incubated with fimbrillin peptide-specific anti-sera prior to the addition to HUVEC. Furthermore, the addition of a peptide corresponding to the N-terminal domain of fimbrillin to HUVEC resulted in an increase in ICAM-1, VCAM-1, and P- and E-selectins, which was maximal at 48 h and similar to that observed for live P. gingivalis. Treatment of P. gingivalis-infected HUVEC with cytochalsin D, which prevented P. gingivalis invasion, also resulted in the inhibition of ICAM-1, VCAM-1, or P- and E-selectin expression. Taken together, these results indicate that active P. gingivalis invasion of HUVEC mediated via the major fimbriae stimulates surface-associated cell adhesion molecule expression. Stimulation of adhesion molecules involved in the recruitment of leukocytes to sites of inflammation by P. gingivalis may play a role in the pathogenesis of systemic inflammatory diseases associated with this microorganism, including atherosclerosis.