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Expression of adhesion molecules by endothelial cells of early human decidua

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Abstract. The expression of adhesion molecules by endothelial cells (EC) of early human decidua was studied with monoclonal antibodies and the immunoperoxidase technique. Although E-selectin, INCAM–110 and VCAM–1 were poorly detected on decidual EC, ICAM–1, P-selectin and DR antigens were highly expressed by these cells, some of which showed high endothelial venule-like morphology. Our results suggest that decidual EC are activated, and are probably involved in the active recruitment of leucocytes.

Key words: Decidua – Endothelial cells – Adhesion molecules – Leucocyte recruitment

Introduction

Pregnancy can be considered an example of semiallogenic transplantation, since the mother and fetus possess different histocompatibility antigens. In contrast to most clinical transplants, however, the fetus is not rejected. Maternal tolerance to the fetus is probably supported by different systemic (Castilla et al. 1989, 1990) and local mechanisms (Rueda et al. 1990). The decidua, as the maternal tissue in contact with fetal trophoblast, appears to play a central role in these local mechanisms, since many immunological activities have been demonstrated in this tissue (Bulmer 1989). Furthermore, the decidua contains many leucocytes (Bulmer 1989; Vargas et al. 1992) which appear to be responsible for these activities, although the mechanisms of recruitment of the high numbers of decidual leucocytes are not known. In general, the arrival of leucocytes to the tissues is regulated by endothelial cells (EC). These cells express certain adhesion molecules which can arrest circulating leucocytes, recruiting them to extravascular tissues (Pober 1988). Although adhesion molecules such as ICAM–2 are constitutively expressed on resting EC and their expression does not change in any situation (Staunton et al. 1989), after inflammatory or immunological stimuli, local cytokine secretion induces EC to express or increase the expression of other adhesion molecules. The inducible adhesion molecules expressed by activated EC include members of the immunoglobulin superfamily, such as ICAM–1 (CD 54; Dustin et al. 1986); VCAM–1 (Osborn et al. 1989) and INCAM–110, which appears to be the same molecule as VCAM–1 (Rice et al. 1990). Members of selectins, (molecules with an N-terminal lectin domain), such as E-selectin (ELAM–1; Bevilacqua et al. 1987) and P-selectin (CD 62; McEver et al. 1989) are also expressed by activated EC.

The large number of leucocytes detected in the normal decidua (Bulmer 1989; Vargas et al. 1992), together with the possibility that this tissue may be able to actively recruit these cells during normal pregnancy in a manner similar to tissues involved in an inflammatory or immune response, prompted us to study the expression of inducible adhesion molecules by the EC of the human decidua.

Materials and methods

Decidua from first-trimester elective vaginal termination of pregnancy (6–9 weeks) was used. The specimens ($n=9$) were obtained from the Clinica El Sur (Malaga, Spain). Frozen sections were treated with mouse monoclonal antibodies (mAbs) against different adhesion molecules (Table 1). The reactivity of the antibodies was

Table 1. List of mAbs used

MAb	Specificity	Source
1E5	E-selectin	Dr. T. Carlos
H18/7	E-selectin	Dr. M.P. Bevilacqua
S12	P-selectin (CD62)	Dr. R.P. McEver
RR1/1	ICAM-1 (CD54)	Dr. T.A. Springer
4B9	VCAM-1	Dr. T. Carlos
E1/6	INCAM-110	Dr. M.P. Bevilacqua
OKIa	HLA-DR	Ortho Diagnostic Systems, N.J.
L243	HLA-DR	Becton–Dickinson, Calif.

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Table 2. Reactivity of mAbs with endothelial cells (EC) and other cells of early human decidua

MAb	Venular EC	Arteriolar EC	Capillary EC	Cells
1E5	−	−	−	−
H18/7	+[a]	−	−	−
S12	+ + + +	+ +	−	−
RR1/1	+ + + +	+ + + +	+ + + +	L, M, DEC
4B9	−	−	−	L, M
E1/6	+[b]	+	−	−
OKIa	+ + + +	−	+ + + +	L, M, DEC
L243	+ + + +	−	+ + + +	L, M, DEC

+ + + +, 75–100% of each type of vessel positive; + + +, 50–75%; + +, 25–50%, +, 5–25%; −, < 5%
L, Lymphocytes; M, macrophages; DEC, decidual cells
[a] In two of nine deciduas
[b] In three of nine deciduas

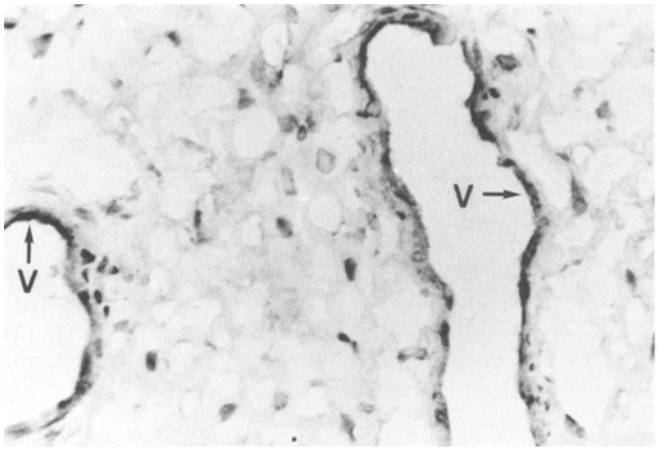

Fig. 1. ICAM–1 positive decidual venules (*V*) in early decidua, × 250

visualized with peroxidase-conjugated rabbit anti-mouse IgG (Sigma, St. Louis, Mo.) followed by diaminobenzidine. Sections were counterstained with haematoxylin.

Results

Our results are summarized in Table 2. The anti-ICAM–1 RR1/1, anti-P-selectin S12 and anti-DR OKIa and L243 mAbs showed widespread, intense reactivity with decidual EC. ICAM–1 was expressed by most of the venular EC, arteriolar EC and capillary EC (Figs. 1, 2), P-selectin by most venular EC, by some arteriolar EC and by no capillary EC (Fig. 3), and DR by most of venular EC and capillary EC but not by arteriolar EC (Fig. 4). Some of the venules which were positive for ICAM–1, P-selectin or DR were similar in morphological appearance to high endothelial venules (HEV; Figs. 2–4). Of the anti-E-selectin mAbs, 1E5 was negative with all the samples, while H18/7 was weakly positive in two of nine specimens, reacting with some venular EC. The anti-VCAM–1 4B9 did not react with decidual EC, while the anti-INCAM–110 E1/6 was positive in only three of nine samples, being weakly detected on both venular EC and arteriolar EC, but not on capillary EC (Table 2). Many mononuclear cells and some decidual cells expressed ICAM–1 and DR antigens. VCAM–1 was detected on mononuclear cells distributed in aggregates.

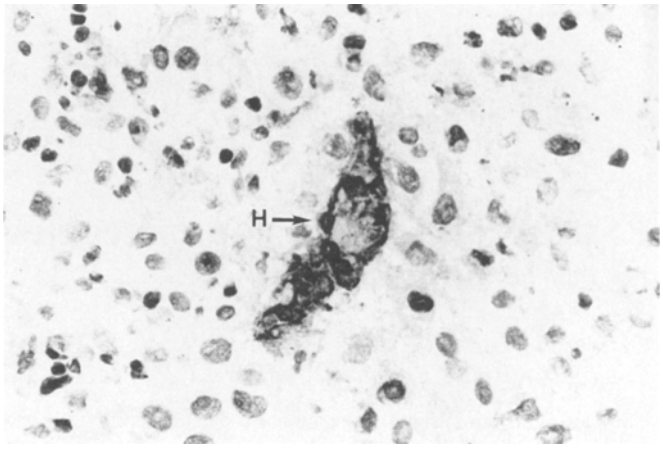

Fig. 2. ICAM–1-positive venule showing morphological characteristics of a high endothelial venule (*H*), × 500

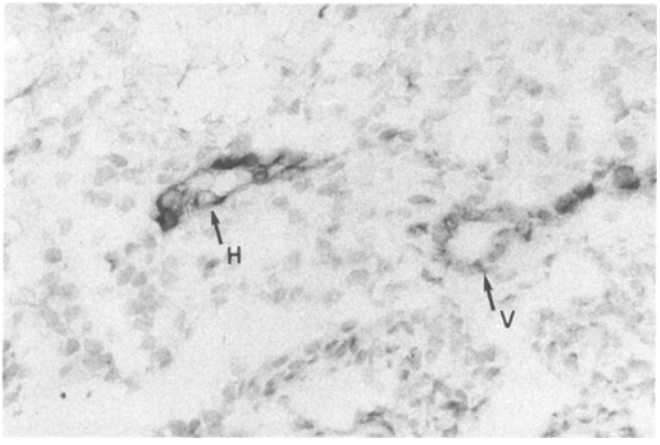

Fig. 3. P-selectin-positive decidual venules (*V*), one showing high endothelial venule-like morphology (*H*), × 250

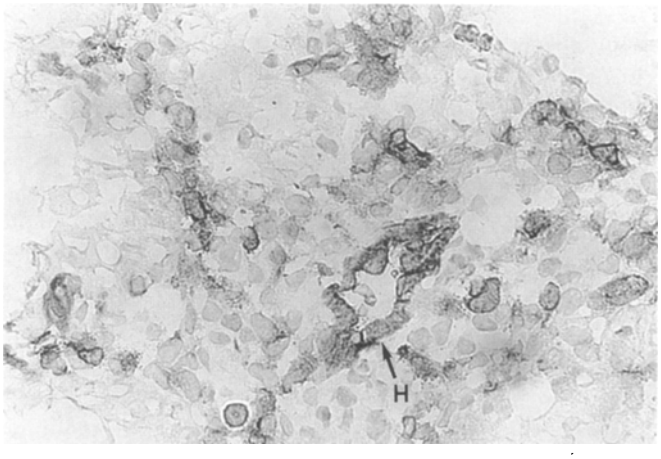

Fig. 4. A DR-positive venule showing morphological characteristics of a high endothelial venule (*H*). DR-positive mononuclear cells are seen in the vicinity, × 250

Discussion

Although ICAM–1, P-selectin and DR antigens are weakly expressed by the vascular endothelium of some normal tissues (Dustin et al. 1986; Mc Ever et al. 1989), the high expression of these molecules by the EC of the early human decidua in terms of the proportion of vessels stained and intensity of staining (Table 2) suggests that these EC are activated (Pober 1988). In agreement with our results, Tabibzadeh and Poubouridis (1990) have found intense expression of ICAM–1 and DR in EC of human endometrium. This suggests that the mechanism that activates EC is already functioning in the endometrial cycle and remains in effect in gestational decidua if pregnancy occurs. This mechanism may be related to local secretion of cytokines (Wegmann 1990). Activated EC may be involved in recruiting leucocytes to the decidua, which would explain the abundance of these cells in this tissue (Bulmer 1989; Vargas et al. 1992). This possibility is supported by the observation that some decidual venules positive for ICAM–1, P-selectin or DR exhibited HEV-like morphology (Figs. 2–4). HEVs, structures detected in lymphoid and inflamed tissues involved in leucocyte recruitment, may have the same role in decidua. In contrast with the high expression of ICAM–1, P-selectin and DR by the decidual EC, the detection of E-selectin, INCAM–110 and VCAM–1 was weak or absent in most of the samples studied (Table 2). This differential expression of adhesion molecules by decidual EC may influence the type of leucocyte selected for recruitment (Springer 1990); CD56+ lymphocytes and macrophages being the most abundant cell types in early decidua (Bulmer 1989; Vargas et al. 1992). The high expression of DR molecules by decidual EC may be involved in the recruitment of T lymphocytes to this tissue. Masuyama et al. (1986) demonstrated the adhesion of T lymphocytes to the DR molecules of interferon activated endothelial cells, and Pober and Contran (1991) proposed that major histocompatibility molecules also function as endothelial leucocyte adhesion molecules for T lymphocytes. T cells, although scarce in early decidua, become more numerous as pregnancy progresses (Vargas et al. 1992).

Unlike the high expression of ICAM–1 and class II–HLA molecules maintained for long periods by activated EC of many tissues, the expression of P-selectin is only transient; after a few minutes this molecule is internalized from the cell membrane (Hattori et al. 1989). This contrasts with the high expression of P-selectin detected on decidual EC (Table 2). Nevertheless, it has been shown that under the effects of certain oxidant radicals, prolonged and enhanced surface expression of P-selectin occurs (Patel et al. 1991). Although in decidua there is a large proportion of macrophages that may be the source of oxidant radicals (Bulmer et al. 1988), we do not know whether these products are secreted in substantial amounts under normal conditions. The counter-receptor for P-selectin is not yet well characterized but there is evidence that it recognizes sialyl-LewisX (SLe^x; Polley et al. 1991), a terminal carbohydrate containing sialic acid and fucose, found in cell membrane glycolipids and glycoproteins. Interestingly, SLe^x has been detected on endovascular trophoblast, the type that colonizes decidual vessels (King and Loke 1988). In this colonization, a phenomenon important for the vascular adaptive mechanisms of the materno-fetal interface (Moll et al. 1975), the expression of P-selectin by decidual EC may play an important role in the recognition of the endovascular trophoblast.

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