Human Reproduction vol.14 no.6 pp.1628–1634, 1999

Increased blood vessel density in decidua parietalis is associated with spontaneous human first trimester abortion

Bruno Vailhé[1,2], Johannes Dietl[2], Michaela Kapp[2], Bettina Toth[2] and Petra Arck[2,3,4]

[1]Université Joseph Fourier, Grenoble, France, [2]Universitäts-Frauenklinik Würzburg and [3]Humboldt Universität zu Berlin, Germany

[4]To whom correspondence should be addressed at: Campus Virchow Klinikum, Medizinische Klinik mit Schwerpunkt Psychosomatik/Biomedizinisches Forschungszentrum, Augustenburger Platz 1, 13353 Berlin, Germany

Spontaneous pregnancy loss affects 15–18% of couples, and a number of potential causes are being discussed. The purpose of the present study was to assess if angiogenic disorders in the decidua of early human pregnancy could be related to spontaneous abortions. First trimester human decidua from elective terminations of normally progressing pregnancies and from missed abortions were investigated immunohistochemically. We quantified vessel density in decidua from normal pregnancies and from abortions by von Willebrand factor (vWF), platelet endothelial cell adhesion molecule (PECAM-1) and CD34 staining. Decidual blood vessel expression of αvβ3 integrin was also investigated. Significant increase ($P < 0.02$) in vessel density was observed in decidua parietalis of abortions, compared to decidua basalis. This increase was detected on slides stained for vWF and CD34, but not for PECAM-1. We observed a 15% increase analysing with vWF and a 77% increase with CD34 staining. αvβ3 integrin expression was not significantly different, neither in decidua parietalis from abortion, nor parietalis from normal pregnancies. Our data suggest that the increased vascularization in decidua parietalis from abortions could reflect complex disorders, such as specific cytokine expressions and hypoxia phenomena during the development of the decidua.

Key words: angiogenesis/decidua basalis and parietalis/human pregnancy/spontaneous abortion

Introduction

Spontaneous abortions in humans are thought to represent rejection of the semiallogeneic fetal unit by activated maternal natural killer (NK) cells and activated macrophages (King and Loke, 1993; Miller and Hunt, 1998). It has been proposed that macrophage-derived tumour necrosis factor-α (TNF-α) stimulates NK cells to produce γ-interferon (γ-IFN) which further activates macrophages, and systemic Th1-type responses may cause abortion via augmenting levels of such cytokines (Raghupathy, 1997). The mechanisms by which the implanted embryo is killed are still unknown. The current paradigm holds that the fetal trophoblast cells, which form the interface between the embryo and maternal tissue, are damaged or killed (Arck and Clark, 1997). Recent published data on murine pregnancy have shown that neither macrophages nor NK cells seemed necessary for TNF-α and γ-IFN to act, therefore the most logical target appears to be the vascular endothelial cell (Clark *et al*., 1998). In mice, these cytokines stimulate surface expression of pro-coagulant and the subsequent clotting process is known to lead to ischaemic damage and depletion of pro-coagulant prevented abortion (Clark *et al*., 1998). These data demonstrate that the vascular supply of trophoblast and implanted embryo appears uniquely sensitive. However, little information is currently available on the morphology and pathology of the human decidual vascular system (Lim *et al*., 1997; Zhou *et al*., 1997a,b). It is known that the vascularization of human decidua is of primary importance in the success of pregnancy (Klauber *et al*., 1997), and vascular disorders may play a role in pathological pregnancies (Roberts and Redman, 1993; Roberts, 1998). The global architecture of the vasculature of decidua was described a few decades ago (Bouda, 1967, 1968, 1969a); these early studies dealt with the possible link between vascular disorders and spontaneous abortion (Bouda, 1969b; De Agustin *et al*., 1971). Nevertheless, until now the decidual microcirculation received poor scientific attention. Nowadays, recently developed antibodies and well-defined immunohistological tools give rise to better results than histological methods. In the present study, our objective was to assess the blood vessel density in human decidua from spontaneous abortions, one major question being which marker to choose to highlight the endothelial cells, taking into account the endothelial cell heterogeneity of this tissue. Three different endothelial cell markers were chosen to investigate decidual blood vessel density: von Willebrand Factor (vWF), platelet endothelial cell adhesion molecule-1 (PECAM-1), and CD34.

vWF is a glycoprotein synthesized in endothelial cells and megakaryocytes (Ruggeri, 1997). It participates in haemostasis by mediating the adhesion of platelets to exposed subendothelium and promoting the formation of a platelet plug at the site of vascular injury. vWF also plays an essential role as a carrier protein for Factor VIII (Wagner, 1990; Ruggeri, 1997). As the expression and storage of vWF is confined to endothelial cells and megakaryocytes, this marker is a useful target to detect blood vessels by immunohistochemistry. The second endothelial marker investigated is PECAM-1 (also referred to as endoCAM or CD31), which is a transmembrane endothelial cell adhesion molecule belonging to the immunoglobulin superfamily (DeLisser *et al*., 1994). The expression of PECAM-1 is confined to the surface of circulating platelets, leukocytes, and the endothelial intercellular junction (Newman, 1997).

Table I. Demographic details of biopsies from two groups of women, either undergoing elective termination of normal pregnancies or undergoing evacuation of the uterus for a primary abortion

Group	*n*	Age (years)	Gestional age (weeks)	No. of prior abortions
Normal pregnancy				
vWF, PECAM or CD34[a]	12	29.6	8.9	–
αvβ3[a]	6	25.5	7.6	–
Abortion				
vWF, PECAM or CD34[a]	15	28.9	8.7	2.4
αvβ3[a]	6	28.3	9.3	2.0

[a]Results of immunostaining two to four tissue samples for each patient. vWF = von Willebrand Factor; PECAM = platelet endothelial cell adhesion molecule.

One of the roles of PECAM-1 could be to modulate the endothelial permeability, thereby modulating leukocyte–endothelial transmigration (Muller *et al*., 1993). The third marker we chose is CD34, which is a glycosylated transmembrane protein expressed on haematopoietic, as well as on a variety of endothelial cells (Fina *et al*., 1990). Its function remains unclear, but it has a possible role in angiogenesis and leukocyte adhesion (Fina *et al*., 1990; Schlingemann *et al*., 1990).

The vascular density (VD) of a tissue can be modulated by angiogenesis, which is defined as the formation of new blood vessels from pre-existing vessels (Risau, 1997, 1998). Angiogenesis is a complex, multifactorial process, which normally does not occur in the healthy adult body, except during regulated physiological situations such as wound healing and in the female reproductive tract (Folkman 1995; Rees and Bicknell, 1998). Many integrins are implicated in angiogenesis (Davis and Camarillo, 1995; Friedlander *et al*., 1995). These molecules are transmembrane heterodimeric cell surface receptors (Clark and Brugge, 1995). The αvβ3 integrin, especially, is likely to play an important role (Varner *et al*., 1997). This integrin has a low expression in quiescent blood vessels, but its expression is highly increased in angiogenic vessels (Brooks *et al*., 1994a,b, 1995). Experiments performed with anti-αvβ3 antibodies showed that this integrin plays a role during neovascularization (Brooks *et al*., 1995; Friedlander *et al*., 1995).

The aim of the present study was to quantify the blood vessel density in human decidua from normal pregnancies and from spontaneous abortions, using a panel of antibodies directed against vWF, PECAM-1 and CD34. The expression of the integrin αvβ3 was also investigated as a putative marker of angiogenesis.

Materials and methods

Patients

First trimester decidual biopsies were collected from two groups of females, (i) undergoing elective termination of normally progressing pregnancies, (ii) undergoing evacuation of the uterus for a primary abortion. Demographic details are given in Table I. Before tissue collection the study was approved by the local ethics commitee. All miscarriage patients were investigated by physical examination and ultrasound and no reasons for the miscarriage, such as uterine abnormalities, infections, genetic abnormalities in the parents or pre-existing medical diseases were found. The use of tissue obtained from curettage of patients suffering from abortions is controversial; however, it is still the only way to evaluate the in-situ situation in human decidua. In the present study we therefore exclusively used fresh tissue samples; any histological signs of tissue damage such as necrosis, old blood clots or infections were excluded from the study. The diagnosis of missed abortion during the first trimester was based on transvaginal ultrasound, decreasing β-human chorionic gonadotrophin (β-HCG) concentrations and absence of vaginal bleeding.

Biopsies

Tissues were washed in phosphate-buffered saline (PBS), pH 7.4 and either routinely fixed in 6% neutral buffered formalin and embedded in paraffin, or snap-frozen in liquid nitrogen and kept at –70°C until use. Cryostat sections were cut at 2 µm, air-dried, fixed in acetone for 10 min and stored at –20°C. Paraffin sections were cut at 2 µm and used for immunohistochemistry. For each patient we examined two to four different tissue samples.

Immunostaining of cytokeratin (CK), vWF, PECAM-1 and CD34

Sections 2 µm thick were stained with a monoclonal antibody (mAb) against pancytokeratin (Clone KL1; Immunotech, Hamburg, Germany) to confirm the presence or absence of invasive trophoblast and proliferating endometrial glands. On this basis, the decidua was classified as decidua basalis (invasive trophoblast or huge proliferating glands present) or decidua parietalis (no trophoblast or proliferating glands present). Consecutive slides were stained with mAb against human vWF (Clone F8/86; Dako, Hamburg, Germany), PECAM-1 (Clone JC/70A; Dako) and CD34 (Clone QBEND10; Dianova, Hamburg, Germany). All subsequent procedures were conducted at room temperature, unless otherwise detailed. Tissue sections were dewaxed in Xylol (Merck, Darmstadt, Germany) and rehydrated through a descending ethanol series. Non-specific endogenous peroxidase activity was blocked by treatment with 3% hydrogen peroxide in methanol for 30 min. Antigen retrieval was performed by microwave boiling in citrate buffer at pH 6.0 for 15 min. Tissue sections were then washed with Tris-buffered saline (TBS; pH 7.4) for 2×5 min and exposed to a non-immune, serum-free protein block (Dako). Cytokeratin mAb was applied at a dilution of 1 in 100 for 60 min. PECAM-1 mAb was applied at a dilution of 1 in 30 for 60 min and vWF mAb at a dilution of 1 in 25 for 60 min. CD34 mAb was a ready-to-use solution and also incubated for 60 min. This was followed by biotinylated multilink anti-mouse mAb for 15 min, and an avidin–biotin–peroxidase detection system (LSAB-Kit; Dako) for a further 15 min. Finally, the sections were developed with diaminobenzidine (DAB; Sigma, Munich, Germany) for 5 min to generate a brown-coloured product and lightly counterstained with haemalum (Roth, Munich, Germany) prior to mounting with Vitro-Clud (Langenbrinck, Emmendingen, Germany). As a positive control, tissue from umbilical cord and endometrium was used. Negative controls were performed by replacing the primary mAb with serum-free protein block (Dako) at the same concentration as the primary mAb.

Immunostaining of αvβ3

Unfortunately, the staining of αvβ3 integrin was not possible on our pool of paraffin sections and therefore performed on a different tissue pool of frozen sections. All subsequent procedures were done at room temperature. Frozen sections were allowed to air-dry for 1 h. Tissue sections were then washed with TBS, pH 7.4 for 5 min and exposed to a non-immune, serum-free protein block (Dako). αvβ3 mAb (clone

LM609; Immunotech) was applied at a dilution of 1 in 100 for 60 min. Tissue from endometrium was used as a positive control. The protocol was then continued as described for the paraffin sections.

Determination of the percentage of blood vessels stained for αvβ3 integrin

Normal pregnancy decidua parietalis and decidua parietalis from abortion were investigated. The percentage of blood vessels stained by αvβ3 mAb was calculated from the number of blood vessels stained for αvβ3 and the total number of blood vessels. The total number of blood vessels was quantified from a CD34 stained serial section.

Vessel counting

The number of blood vessels/mm^2 of tissue was evaluated by two independent observers using a light microscope (Leica, Wetzlar, Germany) with scaled eye pieces pre-calibrated with a slide micrometer, at a magnification of ×250 (×25 objective, with a ×10 ocular), without knowledge of the patient's outcome. Deciduas were frequently heterogeneous in their vessel density. In particular, we observed that the vascularization of the stroma was frequently poor. Thus, for each slide, the blood vessels were counted in the entire tissue section and not only in the areas of highest vascularization. Then, the surface of the tissue section was measured and the mean blood vessel density calculated for each slide. Any brown-staining endothelial cell or endothelial cell cluster that was clearly separate from adjacent vessels was considered as a single, countable vessel. Vessel lumens were not necessary for a structure to be defined as a vessel, and red blood cells were not used to define a vessel lumen. Branching structures were counted as a single vessel. PECAM-1 and CD34 immunostained plasma cells were eliminated from the counts. No statistically sgnificant difference between the counts made by observer I and observer II could be calculated. Therefore we considered the inter-observer reproducibility as satisfactory (Student's *t*-test, $P < 0.05$).

Statistical analysis

Mean scores and SEM were calculated for each group. We used Student's *t*-test to assess significant differences of the mean VD values. $P < 0.05$ was considered significant.

Results

Vessel density assessed by vWF staining

vWF was expressed by decidual vascular endothelial cells of large and small vessels (Figure 1A). Positive staining was observed in both normal pregnancy decidua and decidua from abortions. No significant differences were found between the vascular density of decidua basalis from normal pregnancies and decidua basalis from abortions: the vascular counts varied from 18.9 in normal pregnancy to 19.9 in abortion (Figure 2). In addition, no significant difference was found between normal pregnancy decidua parietalis and decidua parietalis from abortion, where vascular counts ranged from 27.0 to 31.5 (Figure 2). A noticeable difference was observed between the vascularization of decidua basalis from normal pregnancy (VD = 18.9) and decidua parietalis from normal pregnancy (VD = 27.0), but this difference was not significant. However, a significant difference ($P < 0.02$) was observed by comparing decidua basalis from abortion (VD = 19.9) and decidua parietalis from abortion (VD = 31.5). This difference was mainly due to an increased vascularization in decidua parietalis from abortion. In the following experiments, we wanted to confirm these results by staining the endothelial cells for a second marker, PECAM-1.

Vessel density assessed by PECAM-1 staining

PECAM-1 was expressed in large and small vessels in decidua from normal pregnancies and from abortion (Figure 1C and D). However, a weaker staining was observed in the case of abortions (Figure 1D), suggesting a decrease of PECAM-1 expression in decidua from abortion. This was observed in decidua basalis, as well as in decidua parietalis and for all types of vessels. VD was 22.4 in decidua basalis from normal pregnancy, 22.6 in decidua basalis from abortion, 26.9 in decidua parietalis from normal pregnancy and 22.0 in decidua parietalis from abortion (Figure 3). From the results obtained by the vWF and PECAM-1 staining we postulate that the use of only one endothelial cell marker to assess the vascularization of a tissue is not an appropriate method. Results must be confirmed by at least two markers, otherwise it could lead to a misinterpretation of the data. In our case, we suspected that the weaker staining observed in decidua from abortion (Figure 1D) could lead to non-detection of a certain number of blood vessels. Therefore, we chose to assess the vascularization of the deciduas with a third marker, CD34.

Vessel density assessed by CD34 staining

Intense CD34$^+$ staining was expressed by large and small vessels (Figure 1E and F). No difference in staining intensity has been observed between normal pregnancy decidua and decidua from abortions (Figure 1E and F). Vessel counts are depicted on Figure 4. As in vWF and PECAM-1 stainings, we did not observe any significant differences in VD between normal pregnancy decidua basalis (VD = 21.8) and decidua basalis from abortion (VD = 23.2). Interestingly, we observed a difference between decidua parietalis from normal pregnancy (VD = 29.5) and decidua parietalis from abortion (VD = 52.4), but this difference was not significant. With regard to the results obtained with the vWF staining, we did not observe a significant difference between normal pregnancy decidua basalis (VD = 21.8) and decidua parietalis (VD = 29.5). However, our results became highly significant ($P < 0.001$) in the case of abortion (VD = 23.2 for basalis and VD = 52.4 for parietalis). Thus, the CD34 staining confirmed that the balance between the vascularization of decidua basalis and decidua parietalis appeared to be modified in the case of abortion (Figure 1E and F). Vascular densities in human endometrium (Rogers *et al*., 1993; Song *et al*., 1995) ranging between 20 and 50 vessels/mm^2 were found compared to values of 169 and 186 vessels/mm^2 for endometrium in the previously published studies. In our study we took into account the surface area of the glands to establish the vascular density. The value of 169 vessels/mm^2 for CD34 staining, (Song *et al*.,1995), was obtained by manual counting. A value of 186 vessels/mm^2 was obtained (Rogers *et al*., 1993) by an image analysis system. Since it has not been specified by these authors if the gland surfaces have been taken into account, we

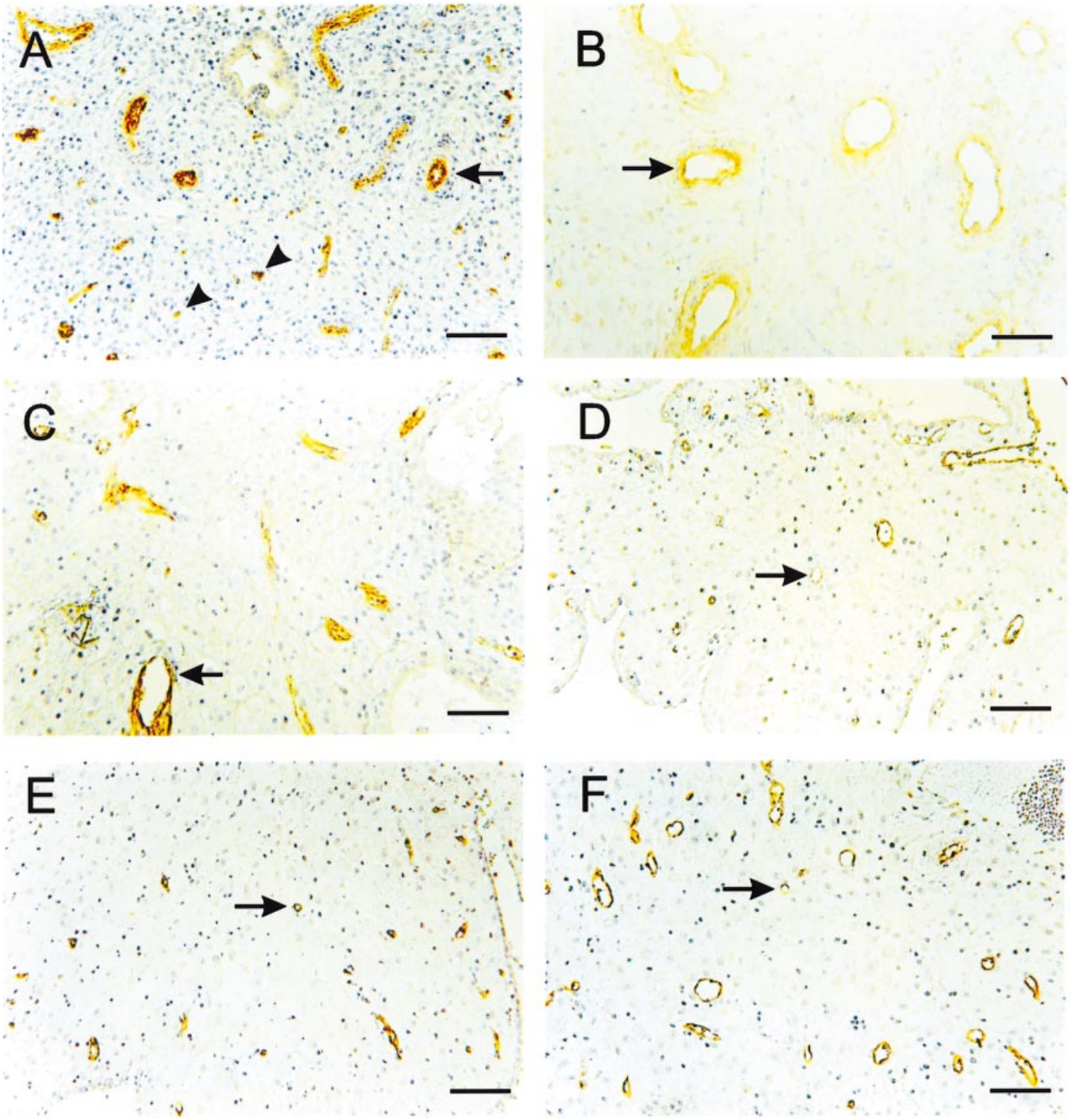

Figure 1. Blood vessels localized in decidua by immunohistochemistry. (**A**) von Willebrand Factor staining. Large vessels (arrow) as well as capillaries (arrowheads) were stained. A representative view of decidua parietalis is shown; similar results were observed in decidua basalis and parietalis, from normal pregnancy and from abortion. (**B**) αvβ3 integrin localization in decidua. An area where blood vessels were stained is shown (arrow). However, vascular staining was heterogeneous and there was no particular relationship between either vessel size or type, decidua type and positive or negative staining. Similar results were observed both in the case of abortion and normal pregnancy. (**C**) Platelet endothelial cell adhesion molecule (PECAM) staining in normal pregnancy decidua. Intense staining of the vessels was observed (arrow) in parietalis and in basalis. (**D**) PECAM staining in decidua from abortion. A heterogeneous staining was observed in parietalis and in basalis. A weakly stained vessel is indicated (arrow). (**E**) CD34 staining in normal pregnancy decidua parietalis. The high quality of this staining allowed the localization of small microvessels (arrow). (**F**) CD34 staining in decidua parietalis from abortion. Many microvessels were observed (arrow), especially in the stroma of decidua. (Note: hot spots of vascularization are shown, when tissue samples were heterogeneous in their vascularization, with some stromal areas devoid of capillaries.) Scale bar = 400 μm.

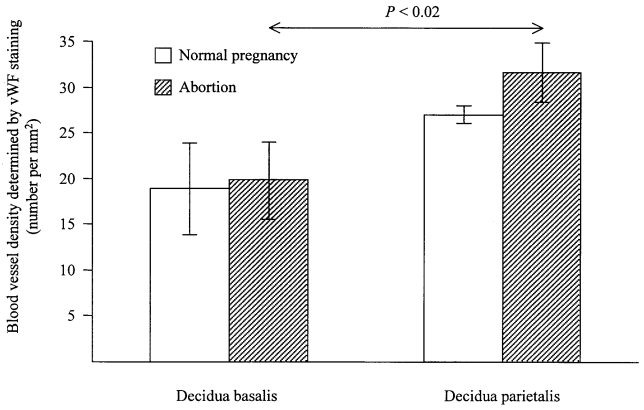

Figure 2. Mean ± SEM blood vessel density as determined by von Willebrand Factor (vWF) staining in normal pregnancy decidua (open bars) and in decidua from abortion (shaded bars). Statistically significant difference between decidua basalis and decidua parietalis from abortion is indicated by the double arrow.

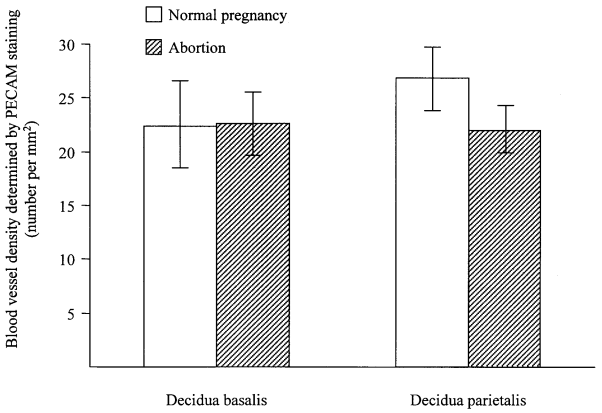

Figure 3. Mean ± SEM blood vessel density as determined by platelet endothelial cell adhesion molecule (PECAM) staining in normal pregnancy decidua (open bars) and in decidua from abortion (shaded bars). No statistically significant differences were observed between either decidua basalis, decidua parietalis, normal pregnancy and abortion.

believe that the differences between the data in the present study and previously published data are methodological in nature.

Expression of αvβ3 integrin in decidua parietalis from normal pregnancy and from abortion

In order to assess if the increased vascularization observed in decidua parietalis from abortion is linked to a specific angiogenic activity of this tissue, we performed an αvβ3 immunostaining (Figure 1B). We assessed the percentage of blood vessels stained for this integrin (Figure 5). No significant differences were observed between the vascular expression of the αvβ3 integrin in normal pregnancy decidua parietalis (39.9% of the blood vessels stained) and decidua parietalis from abortion (26%), as well as between normal pregnancy decidua basalis and decidua basalis from abortion (results not shown).

Discussion

In the present study we did not detect a difference in vascularization between normal pregnancy decidua basalis and decidua

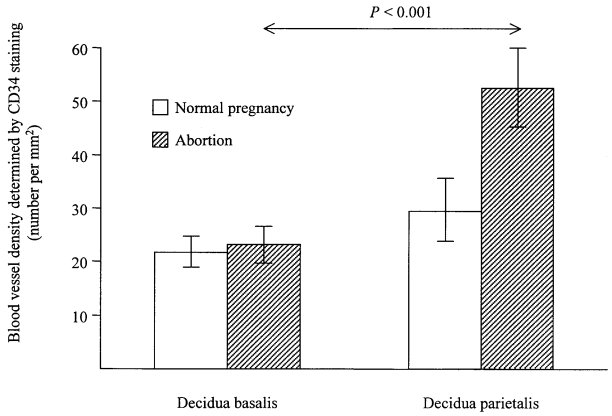

Figure 4. Mean ± SEM blood vessel density as determined by CD34 staining in normal pregnancy decidua (open bars) and in decidua from abortion (shaded bars). Statistically significant difference between decidua basalis and decidua parietalis from abortion is indicated by the double arrow.

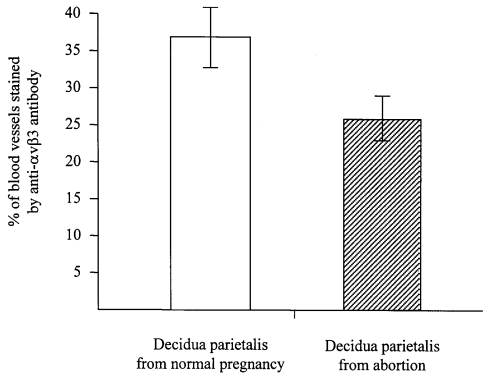

Figure 5. Mean ± SEM percentage of blood vessels stained for αvβ3 integrin in decidua parietalis from normal pregnancy (open bar) and from abortion (shaded bar). No statistically significant difference was observed between decidua parietalis from normal pregnancy and from abortion.

basalis from abortions. However, we observed a dramatic increase in vascularization in decidua parietalis from first-trimester human spontaneous abortions, depending on the marker used to detect the blood vessels. Moreover, we did not observe an increase in the percentage of blood vessels stained for αvβ3 integrin. The point of interest is certainly to determine if the increased vascularization observed in decidua parietalis from abortions is a cause or a result of the failing pregnancy.

Endothelial cells are phenotypically heterogeneous (Thorin *et al.*, 1997). Therefore they are also heterogeneous in their immunoreactivity (Kuzu *et al.*, 1992), thus justifying the choice of a panel of different markers to assess the vascularization of a tissue. Our vascular counts obtained with different immunostainings clearly support this observation. CD34 has been investigated in the assessment of endometrial vascularization (Rees *et al.*, 1993; Rogers *et al.*, 1993; Song *et al.*, 1995; Hickey *et al.*, 1996), but very few studies used it as a vascular marker in first trimester human pregnancy (te Velde *et al.*, 1997). Our observation that, in each case, the blood vessel density is higher when detected by CD34 compared to vWF is in agreement with other authors (Song *et al.*, 1995). It is possible that when using antibodies against vWF or PECAM

some vessels have been missed due to poor antibody or antigen availability. However, this does not explain the discrepancy in vessel density between our study and previous studies by Rogers' and Song's groups, because this discrepancy is exclusively observed in CD34 stainings. vWF is expressed by the decidual endothelium (Grimwood *et al*., 1995), and it has been shown that in human endometrium vascular staining for vWF is heterogeneous, with some vessels devoid of any positive staining (Au and Rogers, 1993). Furthermore, other studies have shown changes in the immunoreactivity of vWF during the menstrual cell cycle (Zhu and Gu, 1988). However, the results we obtained with both vWF and CD34 staining showed a significant increase in the vascularization of decidua parietalis from abortion. The concentration of blood vessels stained for PECAM-1 was not different in normal pregnancy decidua parietalis and in decidua parietalis from abortion, suggesting a decrease of PECAM-1 expression in decidua from abortion. We observed a heterogeneous staining of PECAM-1 in decidua from abortion, with some weakly stained vessels. However, we did not observe such a weak staining in normal pregnancy decidua. This confirms the previous observations (Haynes *et al*., 1997; Ruck *et al*., 1994) where an intense immunostaining of PECAM-1 in endothelium of early normal pregnancy decidua was found, demonstrating the pertinence of the use of this marker to assess the blood vessel density in this tissue.

Our data suggest a causal link between the increased vascularization observed in decidua parietalis and the phenomenon of spontaneous abortion. We observed no differences between normal pregnancy decidua and decidua from abortion regarding the angiogenic activity assessed by αvβ3 integrin staining. This observation allows us to postulate that angiogenesis is not occurring in the decidua at the moment of abortion. The expression of αvβ3 integrin in human endometrial vasculature and glands has been reported and investigated as a sign of angiogenesis (Hii and Rogers, 1998). Our data suggest that the increased blood vessel density observed in decidua parietalis from abortion could reveal intrinsic vascular disorders, linked with the development of the decidua, and thus with causal effects. However, very little is known about the mechanisms of angiogenesis in the endometrium, and some arguments support the hypothesis that these mechanisms could differ from the classical mechanisms known as 'sprouting angiogenesis' (Goodger and Rogers, 1995). Furthermore, as we did not observe a significant increase in vascularization of decidua basalis, the hypothesis of a causal link between the increased vascularization of parietalis and abortion remains to be investigated in depth. If the increased vascularization we observed in decidua parietalis from abortion reflects an attempt of the mother to rescue the pregnancy, why this is not the case in decidua basalis? It was found that E-selectin was only detectable on blood vessels from normal pregnancy decidua basalis (Burrows *et al*., 1994), and not in normal pregnancy decidua parietalis. We confirmed this observation (results not shown). These results strongly suggest that the vessels of decidua basalis are phenotypically different from the vessels of decidua parietalis. Even if the role of the E-selectin is still not well understood, observations suggest that this molecule is most likely involved in angiogenesis *in vitro* (Nguyen *et al*., 1993) and *in vivo* (Koch *et al*., 1995). Therefore, these data suggest structural and functional differences between the blood vessels of normal pregnancy decidua basalis and decidua parietalis. Thus, even if these differences remain to be characterized in depth, it can be assumed that the ability of endothelial cells from decidua basalis and decidua parietalis to react to a particular pathophysiological situation could be different.

Our results could also be considered as a consequence of the abortion. It was reported that TNF-α, which belongs to the Th1 cytokine family, is present at the feto-maternal interface, (Lea *et al*., 1997) and Th1 cytokines are associated with spontaneous abortion (Raghupathy, 1997). It has been reported that PECAM-1 expression can be decreased by inflammatory cytokines such as TNF-α and IFN-γ (Rival *et al*., 1996; Stewart *et al*., 1996). This decrease of PECAM-1 expression at endothelial cell–cell contacts could result in a reduction of polymorphonuclear cell migration across the endothelial cell monolayer (Rival *et al*., 1996). Furthermore, PECAM-1 could be involved in the regulation of capillary morphogenesis, because of its localization and expression in angiogenic blood vessels (Berger *et al*., 1993). However, its precise role in angiogenesis in general and in reproduction is still unclear (Dejana and Lostaglio, 1996; DeLisser *et al*., 1997). The earliest event in activated endothelium is usually an increase in vascular permeability, to accelerate the delivery of nutrients, oxygen and perhaps leukocytes rather than by making new blood vessels (Risau, 1998); this further supports the suggestion that the increased vascularization we observed is not a consequence of Th1 activity at the feto-maternal interface. Therefore, we can postulate that a decrease of PECAM-1 expression could rather be a consequence of abortion.

In conclusion, further investigation is needed to assess if the increased vascularization observed in decidua parietalis from abortion is directly linked with causal effects, for example problems during the development of the decidua, or if it is a consequence of tissue damage during the course of the abortion. Our data suggest vascular disorders that could be linked with both.

Acknowledgements

This work was supported by grants from the Deutsche Forschungsgemeinschaft (Ar 232/8-1/Di 390/3-1), IZKF, Julius-Maximilians-University Würzburg (B8) and UFF, Humboldt University Berlin (98-705).

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Received on October 28, 1998; accepted on February 15, 1999