Mini Review

In human placental bed, at the feto maternal interface, the extravillous trophoblastic cells invade not only the decidua but also the subendometrial or Junctional Zone (JZ) myometrium [1-3]. The interstitial and endovascular migratory cells in the vessels wall were later confirmed to be trophoblastic in origin [4].

Brosen et al. suggested that the “physiological change” of spiral arteries in the pregnant uteri was a result of the destructive action of invading trophoblast on vascular smooth muscles and elastic membranes [5]. Later, a maternal contribution had to be considered since some changes in the maternal vessel wall precede the antidromic migration of trophoblast along the vessel lumen. Some researchers believe that the local intravasation of interstitial trophoblast is more likely [6].

The four steps in which remodeling takes place is well documented (Figure 1) [7,8]. The first step is the decidua associated remodeling. Perivascular sheaths of swollen decidual cells (streeter’s column) appear as early as postovulatory day 11[3]. These swollen perivascular cells may be derived from vascular smooth muscles. As early as 9 weeks the uterine decidual natural killer cells secrete Vascular Endothelial Growth Factor (VEGF), Placental growth Factor (PLGF) and angiopoietins [9,10]. This leads to vacuolation and disorganization of vascular intima and endothelial cells (Figure 1A & 1B). In JZ myometrium, since the natural killer cells are absent, the presence of interstitially invading trophoblast may help the release of VEGF and angiopoietins [9,10]. This is evidenced by the fact that the interstitial trophoblast invades the JZ at 8 weeks.

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This is followed by the actual trophoblastic invasion and intra-arterial migration (Figure 1C & 1D). Invasion follows an interstitial and an endovascular course. The endovascular course happens in spiral arteries but never in veins. Intersitial trophoblast, but not endovascular, subsequently fuses to form multinuclear giant cells [11]. Though the multinuclear giant cells appear more striking but it is the mononuclear cytotrophoblast that is most invasive and it occupies extensive area of uterine wall within a short time. An overwhelming number of basophilic mononuclear cells occupy the space between the smooth muscles of JZ myometrium. Quantitative study reveals that their distribution is at the center at 8 to 14 weeks and towards a biphasic distribution at 16-18 weeks. Thus they follow a ring like pattern towards the periphery of placental bed [12]. It is thought that after their fusion to form giant cells they lose some potential of invasion. During endometrial decidualization a selective breakdown of extracellular matrix components occurs independent of trophoblastic action.

The third step is trophoblast associated remodeling when the trophoblast cells are actually incorporated into the arterial wall (Figure 1E). This vascular incorporation is initiated by the penetration of the endothelium. Electron micrograph revealed that the trophoblast penetrates between the healthy endothelial...
cells and cross the underlying basement membrane. The smooth muscle penetration ultimately leads to its replacement by trophoblast embedded within a fibrinoid matrix, probably secreted by the trophoblast itself [13].

The intraluminal trophoblasts now assume a spider-like shape because of increasing accumulation of fibrinoid materials around the cell processes. As a rule, the intraluminal trophoblast remains mononuclear or at the most become binuclear. This is a contrast to the interstitial trophoblast.

The fourth step reendothelialization definitely occurs (Figure 1F). It is not clear whether the maternal vascular lining is repaired by endothelial remnants which were still present after the intramural invasion or whether a new endothelial covering is derived from circulating endothelial progenitor cells [14]. The increase in placental oxygen tension has been correlated with trophoblastic migration (Figure 2).
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Conflict of Interest

Authors have declared that no competing interests exist.

References