Core Curriculum in Perinatal Pathology

Chapter 3

Decidua

Decidualization process
Stimuli for decidualization
  cAMP
  PGE₂
  Relaxin

Cells involved during decidualization
  Decidualized stromal cells (DSC)

Morphology of DSC
Functions DSC
  Molecules secreted by DSC
    Prolactin
    Insulin growth factor binding protein-1 (IGFBP-1)
    Tissue factor (TF) / Plasminogen activator inhibitor (PAI-1)
    Cytokines
    Cell surface expression and adhesion molecules

Non-resident immune cells
  Monocytes/macrophages
  Decidual natural killer cells (dNK)
Objectives

Our understanding of the decidua, the specialized tissue that plays a significant role in pregnancy, has changed significantly over time. Early descriptions have been replaced by a better understanding of the molecular and associated morphological changes.

The purpose of this chapter is to:

1) Review decidualization and molecular factors that regulate this process.
2) Describe the concept of decidual stromal cell (DSC), and review its molecular and morphological characteristics.
3) Review the other endometrial cell populations that play a significant role in implantation and endometrial response to trophoblastic invasion.

Decidualization


Decidualization can be seen as early as day 23 (ten days after the peak of the luteinizing hormone surge). Spiral arteries of the endometrium first become prominent at this time. Stromal cells surrounding the spiral arteries become increasingly eosinophilic and enlarged as the differentiating effect of progesterone transforms these cells into predecidual cells. Progressive decidualization prepares the uterine lining for implantation and the invasive trophoblast.

Immediately after implantation, the decidua impedes the movement of invasive trophoblast both by forming a physical barrier and by generating cytokines that promote trophoblast attachment rather than invasion. Then the fate of invasive trophoblast is determined by the proinvasive factors and the inhibitors of invasion produced by decidua. If invasive forces are insufficient, implantation cannot occur. In the absence of pregnancy, the nonreceptive decidualized endometrium is shed.

Decidualization can be initiated by the ‘downstream’ messenger cyclic adenosine monophosphate (cAMP), prostaglandin E2 (PGE2) and relaxin. At the time of decidualization, increased cytokine production leads to the migration of immune
cells into the endometrium, of which the most important are monocytes and decidual natural killer (dNK) cells. Immune competent cells have a specific role in the preparation of endometrial receptivity. Besides cellular changes, decidualization creates an important extracellular matrix (ECM) composed mainly of laminin, heparan sulphate proteoglycans and type IV collagen.

**STIMULI FOR DECIDUALIZATION**

Three main factors play a significant role in the decidualization process. They are:

1) Cyclic adenosine monophosphate (cAMP)
2) Prostaglandin E₂ (PGE₂)
3) Relaxin

**Cyclic adenosine monophosphate (cAMP)**

*Cyclic AMP* is an intracellular second messenger that allows both the transmission and amplification of signals within cells (*GELLERSEN, ET AL., 2003*). *Progesterone* is essential for decidualization and increased intracellular concentrations of cAMP are critical to this process.

**Prostaglandin E₂ (PGE₂)**

*Cyclooxygenase-1 (COX-1)* is constitutively expressed in most tissues, whereas cyclooxygenase-2 (COX-2) expression is inducible. COX-2 is induced at the time of blastocyst implantation. In the normal menstrual cycle, cyclooxygenase expression within the endometrium has been located to both stromal and glandular compartments, with the highest concentration in the glands. This suggests COX-2 is involved in both the processes of menstruation and implantation (*KANG, ET AL., 2005; MAKINO, ET AL., 2007*).

**Relaxin**

*Relaxin* is a heterodimer of two peptide chains of 24 and 29 amino acids that are linked by disulfide bridges (*BRYANT-GREENWOOD, ET AL., 2007*). It may be related to insulin. It is found in several human reproductive tissues including the ovary and endometrium. During the proliferative and secretory phases, it is expressed in the endometrial glands and surface epithelium. Relaxin levels rise after ovulation as a result of its production by the corpus luteum. In the absence of pregnancy it declines at menstruation. It is associated with upregulation of collagenase in fibroblasts and may affect extracellular matrix modeling.
**Figure 3-1. Implantation site.**
Macroscopic images of a hysterectomy specimen from a 28-year-old woman with cervical carcinoma. The embryo was two weeks post conception.
A) The lining of the uterus is yellow and edematous because it is mostly composed of decidua. The red swelling is the implanted blastocyst.
B) Close up image of the implanted blastocyst. Vascularization around the implantation site is prominent.

**Figure 3-2. Microscopic image of the case illustrated in Fig. 3-1.**
1) Blood clot sealing the implantation site. 2) Cytotrophoblast. 3) Two layer embryo. 4) Early chorionic villus (tertiary). 5) Decidua surrounding the implanted embryo. 6) Endometrial glands. *Hematoxylin and eosin. X100.*
FIGURE 3-3. Different appearances of decidual tissue.
A) Decidua without edema from the case in Figs. 3-1 and 3-2: 1) Luminal epithelial cells lining the endometrial cavity. 2) Decidual stromal cells. Cytoplasmic branches of decidual stromal cells are not visible due to the compactness of the surrounding stroma. 3) Lymphocyte. 4) Decidual blood vessel.
B) The appearance of conventional decidual cells in a standard section. This sample is from a term pregnancy. The decidual stromal cells appear as large, round or oval with their cytoplasm filled with secretory products and rough endoplasmic reticulum. *Hematoxylin and eosin. X100.*