Comparative morphometric characteristics of eutopic and ectopic endometrial cells in patients with endometriomas

Svetlana Dubrovina
The pathogenesis of early-onset endometriosis has recently been revisited, sparked by the discovery of endometrial stem/progenitor cells and the concept that maternal pregnancy hormone withdrawal following delivery induces uterine bleeding in the neonate. The neonatal uterus has a large cervix to corpus ratio which is functionally blocked with mucous, supporting the concept of retrograde shedding of neonatal endometrium. Only 5% show overt bleeding. During the neonatal and prepubertal period, shed endometrial stem/progenitor cells are postulated to survive in the pelvic cavity in the absence of circulating oestrogens supported by niche cells also shed during neonatal uterine bleeding.

Perhaps those that develop early onset endometriosis may have had larger volume bleeds, with more endometrial stem/progenitor cells finding their way into the peritoneal cavity. Or, the fundamental differences in the endometrial stem/progenitor cell populations that predispose for endometriosis, such as carrying one of the susceptibility alleles recently identified for endometriosis risk


The identification of markers for epithelial progenitor cells (eEPC) has been technically more difficult to achieve, but several recent studies have now hypothesized that eEPC are located in the basalis.

Stage-specific embryonic antigen-I (SSE-I), a marker of basalis epithelial cells, was also present in endometriotic lesions, confirming that cells from the basalis contribute to the pathogenesis of endometriosis.

Purpose of the study was to examine morphometric characteristics of eutopic and ectopic endometrial cells with endometriosis.

Samples were obtained from 51 women. The thickness of slices was 4 mm. The resulting sections were stained in the usual manner with hematoxylin-eosin and subjected to optical microscopy using immersion objective with a total optical power of 10 x 100.

Data are presented as the mean ± standard deviation and were analyzed by the Pearson nonparametric correlation to indicate statistical differences.
Feature of eutopic and ectopic endometrium.
Studied parameters

- The thickness of the gland
- The core area
- The number of nucleoli in the nucleus
- The thickness of the cytoplasmic membrane
- The thickness of the nuclear membrane
- The thickness of the secretory parts of the cell
- Average brightness
- The total brightness
- The average density of the nucleus
- The total density of the nucleus
- The diameter of the core
The thickness of the glandular cells (µm)
Characteristic changes in the area of the nucleus (m2)
Characterization of the cytoplasmic membrane thickness (µm2)

Eutopic

Ectopic

Statistical Significance: Р < 0.05
The thickness of the nuclear membrane (µm)
The thickness of the secretory part of the gland (µm)
The characteristics of the average brightness and the density of nuclei.
The diameter of the core and the number of nucleoli.

- The diameter of the core:
  - Eutopic: 0.000043
  - Isotopic: 0.000047

- The number of nucleoli:
  - Eutopic: 2.4
  - Isotopic: 4.9

Р > 0.05, Р < 0.001
Change in the almost all researched markers indicates an increase in cell proliferation activity of ectopic epithelium. Our findings suggest different ways of developing and pathogenetic aspects of proliferative processes in eutopic and ectopic epithelium in patients with endometriomas.
Mesenchymal stem cells (MSC) from peritoneal lesions and ovarian cyst represent different tissue types, migration, invasion, and proliferation ability. Ecto-MSC from an ovarian cyst showed increased proliferation, migration, and invasion with respect to Euto-MSC deriving from the same patient.

With a change in environment following retrograde menstruation potentially altering both paracrine and endocrine signalling, it is likely that a number of epigenetic changes arise in ectopic endometrium, consequently giving rise to the pathology of endometriosis.

1. Munro SK, Farquhar CM, Mitchell MD, Ponnampalam AP. Epigenetic regulation of endometrium during the menstrual cycle Mol Hum Reprod 2010;16(5):297–310
It also defines a new theory for the etiology of endometriosis – ectopic transdifferentiation of stem cells. Bone marrow derived stem cells (BMDCs) can contribute to endometriosis, perhaps explaining the occurrence of disease outside of the peritoneal cavity. BMDCs migrated and differentiated into eutopic and ectopic endometrial cells, although the contribution was very modest. They also could be source of cells for monthly endometrial regeneration. However, BMDC were more likely myeloid cells rather than bone marrow-derived stem cells.

Acknowledgements

My co-authors: Krasililnikova Lily, Gimbut Vitaly, Areshuan Knarik, Berlim Julia, Bychkova Anna, Lemeshko Svetlana, Mazhugin Vladimir, Dmitry Lebedev and Dr. med. Jochen Ruby, Head of Business Unit Women's Health Gynecologist & Obstetrician in Bayer HealthCare Pharmaceuticals for their input in editing the presentation.
Thank you for attention