Endometriosis-stem cell evaluation

A Thesis
Submitted for partial fulfillment of the master degree in obstetrics & gynecology

BY

Ahmed Mouner Ibrahim

(M.B.BCH,)
Resident of Obstetrics & Gynecology
Al-Azhar University(Assuit)
Under supervision of

Prof. Mahmoud Sayed El Edessy

Professor and head of department of Obstetrics & Gynecology
Faculty of medicine
AL-Azhar University(Assuit)

Prof. Magdi Abd El Mohsen Olama

Professor of Obstetrics & Gynecology
Faculty of medicine
AL-Azhar University(Assuit)

Assistant Prof. Dr.Hala Naguib Hosni

Assissant Professor of pathology department
Faculty of Medicine, Cairo University

Dr. Mohamad Abd El Satar Mohamad

Lecturer of Obstetrics & Gynecology
Faculty of medicine
AL-Azhar University(Assuit)

Faculty of medicine
AL-Azhar University (Assuit)
2012-1433

Acknowledgement

A special tribute and appreciation to:

Prof. Dr. Mahmoud Sayed El-edessy

Professor of obstetrics and gynecology, faculty of medicine, Al-Azhar university for his active guidance and support all through the whole work and for dedicating much of his precious time to accomplish this work.

I would like also to express my deep thanks to:

Prof. Dr. MagdyAbd El Mohsen Olama

Professor of obstetrics and gynecology, faculty of medicine, Al-Azher university for his meticulous supervision, generous help, sincere advice and his great effort.

I would like to express my sincere gratitude to:

Prof. Dr. HalaNaguib Hosni

Assistant Professor of Pathology, Faculty of Medicine, Cairo University for her great support and continuous encouragement pushed me to produce good valuable work.

I would like also to express my deep thanks to:

Dr. Mohammad Abd El satar

Lecturer of obstetrics and gynecology faculty of medicine AL-Azhar university (Assuit) for his meticulous supervision, his great support and sincere advice.

Ahmed Mouner

Contents

AMH	anti-Müllerian hormone
AFC	American Fertility Society
ASRM	American Society for Reproductive Medicine
ASCs	Adult stem cells
BMHSCs	Bone marrow hematopoietic stem cells
CA125	Cancer antigen 125
CA19-9	Cancer antigen19-9
COX-2	Cyclooxygenase type 2
CS	Cesarean section
E2	Estradiol
EBs	Embryoid bodies
EC	Embryonal carcinoma
EISS	International stem cell score
EG	Embryonic germ cell
EPC	Endothelial progenitor cells
ESCs	Embryonic stem cells
HESCs	Human embryonic stem cells
HLA	Human leukocyte antigen
HSC	Hematopoietic stem cells
IL-1	Interleuken-1
IL-6	Interleuken-6
IL-8	Interleuken-8

LIF	Leukemia inhibiting factor
IVF	Invitro fertilization
M Ab	Monoclonal antibodies
MCP-1	Monocyte chemoattractant protein-1
MSCs	Mesenchymal stem cells
NSAIDs	Nonsteroidal anti-inflammatory drugs
NOD	Non-obese diabetic
NK	Natural killer
PG	Primordial germ cell
OSE	Ovarian surface epithelium
PCR	Polymerase chain reaction
PDMCs	Placenta-derived multi-potent cells
PGE2	Prostaglandin E2
RANTES	Regulated on activation, normal T-cell expressed and secreted
RCT	Randomized controlled trials
SC	Stem cell
SCID	Severe combined immunodeficiency
SP	Side population
SSEA	Stage specific embryonic antigen
TA	Transit amplifying cells
TCDD	Tetrachlorodibenzo-p-dioxin
TNF	Tumor necrosis factor
UGS	Urogenital sinus
UCB	Umbilical cord blood

VEGF	vascular endothelial growth factor

List of figures

List of tables

Introduction

Introduction

Endometriosis is a chronic benign gynecological disease characterized by the presence of endometrial glands and stroma outside the uterine cavity. The consequences of endometriosis often include pelvic pain and infertility. The incidence of the disorder is between 6% and 10% of all women and 35–50% of women with pelvic pain and infertility (Sasson et al 2008).

The origin of endometriotic implants and the pathogenesis of endometriosis has long been an area of active investigation. Multiple hypotheses have been explored, including:

• Retrograde menstruation theory: This theory is the most widely accepted and postulates that endometriotic implants arise from retrograde menstruation of endometrial tissue through the fallopian tubes into the peritoneal cavity (Sampson et al 1927).

• Coelomic metaplasia theory: This theory proposes that endometriosis develops from metaplasia of the cells lining the visceral and abdominal peritoneum (Gruenwald et al 1942). Some undetermined stimulus is believed to induce metaplastic changes in the peritoneal lining, resulting in endometrial implants.

• Embryonic rest theory: This theory proposes that the presence of endometrial tissue when subjected to the appropriate stimulus.

• Lymphovascular metastasis theories: Sampson suggested that endometrial cells could spread to ectopic sites via lymphatic and hematogenous spread (Sampson et al 1927).

Although there is evidence for each theory, the clinical manifestation of endometriosis and the presence of endometrial tissue outside the uterine cavity is probably the end point of a combination of several aberrant biological processes. For instance, retrograde menstruation may occur in a woman with an improper immune response and a genetic predisposition to develop endometriotic lesions, possibly in the setting of an aberrant environmental milieu (Sasson et al 2008).

Briefly, the mechanisms required include attachment of endometrial cells to the pelvic peritoneum, invasion into the mesothelium, and survival and proliferation of the ectopic endometrial cells (Jensen et al 2010).

Stem cells, the endometrium, and endometriosis ectopic endometrial growth in the many models used for the study of endometriosis (Sasson et al 2008).

Leyendecker et al 2002. Showed that significantly more basalis layer was shed in the menstrual flow, suggesting an increased number of stem cells in this layer that can result in a propensity for endometriosis.

Endometriosis was generated experimentally by ectopic wild-type endometrial implantation in the peritoneal cavity of hysterectomized LacZ transgenic mice.

Stem cells are undifferentiated cells that have the ability to self-renew as well as to produce more differentiated daughter cells (Gargett et al 2007). Broadly, they can be divided into two categories: embryonic and adult. Embryonic stem cells are found in the inner cell mass of the blastocyst. Adult stem cells, derived from postembryonic cell lineages, have been described in a number of different organ systems and have been best characterized in the hematopoietic system (Gargett et al 2007).

Embryonic and adult stem cells are classified by their ability to differentiate into cells of different cell lineages. Differentiation is defined as a change in cell phenotype because of expression of genes associated with cellular function rather than cell division.

Totipotent stem cells are fully undifferentiated and able to generate all embryonic germ layers (endoderm, mesoderm, and ectoderm) aswell as the extra-embryonic tissues (trophoblast, placenta, and extra-embryonic membranes); the zygote is representative of this cell. The embryonic stem cells, in turn, are pluripotent stem cells that lie along a spectrum of differentiation and can produce cells of all three germ layers, but not the extra-embryonic tissues. As stem cells undergo differentiation and their cell lineages become more restricted, they are described as multipotent because they can produce multiple cell types within the same germ cell lineage, or unipotent, differentiating into a single cell lineage (Trounson et al,2006).

Adult stem cells reside in an anatomic structure called the niche (Li et al 2005). The stem cell niche is a microenvironment of surrounding support cells that signal to the stem cell population. The niche cells provide signals that maintain stem cells in an undifferentiated state, protecting them from differentiation, proliferation, and apoptotic cues.

Maintenance of the stem cell population requires cellular self-renewal, that is, the capacity to generate identical daughter cells, which can happen through asymmetric or symmetric division. In an asymmetric division, one stem cell produces an identical daughter cell and a more differentiated daughter, whereas in a symmetric division it produces two daughter stem cells or two transit amplifying (TA) progenitors. TA cells undergo repetitive cycles of cell divisions to increase in number while progressively acquiring markers of the differentiated cell type; consequently, they lose the ability for self-renewal.

The human endometrium of the uterus comprises the endometrial mucosal lining, which is a highly regenerative tissue. It is composed primarily of two cell types—the epithelial cells (luminal and glandular). And the supporting mesenchymal cells (stromal cells) as well as

endothelial cells and leukocytes (Kayisli, et al 2004). The endometrial–myometrial junction is irregular with no submucosal tissue to separate endometrial glandular tissue fromthe underlying smooth muscle of the myometrium (Uduwela, et al 2000).

Functionally, the endometrium is composed of two layers—the outer functionalis layer and the inner basalis layer. The functionalis, comprising the upper two thirds, is composed of dense glandular tissue surrounded by a loose connective stroma. The inner basalis layer rests on themuscular subendometrial myometrium and contains primarily the base of the glands, dense stroma, and large vessels. This layer serves as a germinal compartment for generating the new functionalis each month (Spencer et al 2005).

So, more researches are needed to find out the relation of these endometriotic cells and occurrence of endometriosis. Assessing of the presence of stem cells in the endometrium and endometriotic cells may be a clue to know more about the pathogenesis of endometriosis.