Pathophysiology of Endometrial Hyperplasia

Learning Objectives

- At the end of the session student should be able to:
- Define dysfunctional uterine bleeding.
- What are the causes of DUB.
- Define endometrial hyperplasia.
- Describe the different morphological types of endometrial hyperplasia.

Introduction

- Dysfunctional uterine bleeding (DUB) is defined as ABNORMAL uterine bleeding with no demonstrable organic cause, genital or extragenital.

- Diagnosis of EXCLUSION

- Patients present with “abnormal uterine bleeding”
- DUB occurs most often shortly after menarche and at the end of the reproductive years.

- DUB is most frequently associated with chronic anovulation.
- Heavy menses, prolonged menses, or frequent irregular bleeding are the most common complaints.
- Up to 20% of women will experience irregular cycles in their lifetimes.

CAUSES (DUB)

- Anovulatory Cycle
- Inadequate Luteal Phase
- Oral Contraceptives
- Menopause
- Post-Menopause
Anovulatory Cycles

- Anovulation results in excessive and prolonged estrogenic stimulation without the counteractive effect of the progestational phase that follows ovulation.
- In most women anovulatory cycles have no obvious cause, occurring most likely due to subtle hormonal imbalances.

- A primary lesion of the ovary
  - Granulosa-theca cell tumors or polycystic ovaries
  - A generalized metabolic disturbance, such as marked obesity, severe malnutrition, or any chronic systemic illness.
- Less commonly
- An endocrine disorder, such as thyroid disease, adrenal disease, or pituitary tumors.

INADEQUATE LUTEAL PHASE

- Inadequate corpus luteum function resulting in low progesterone, with subsequent early menses.
- The condition often manifests clinically as infertility, with either increased bleeding or amenorrhea.

ORAL CONTRACEPTIVES

- Ovarian steroids induce a wide variety of endometrial changes.

  - A common response pattern
  - Discordant appearance between glands and stroma, usually with inactive glands amid a stroma showing large cells with abundant cytoplasm reminiscent of the decidua of pregnancy. When such therapy is discontinued, the endometrium reverts to normal.

MENOPAUSAL AND POSTMENOPAUSAL CHANGES
Anovulatory cycles and uninterrupted estrogen production can induce mild hyperplasias with cystic dilation of glands. If this is followed by complete ovarian atrophy and loss of stimulus, the cystic dilation may remain, while the ovarian stroma and gland epithelium undergo atrophy. In this case, so-called cystic atrophy results.

Endometrial Hyperplasia
- An increased proliferation of the endometrial glands and stroma, resulting in an increased gland-to-stroma ratio when compared with normal proliferative endometrium.
- It is an important cause of abnormal bleeding.

Endometrial Hyperplasia
- Endometrial hyperplasia is associated with prolonged estrogen stimulation of the endometrium.

Causes
- Anovulation, increased estrogen production from endogenous sources, or exogenous estrogen.

Conditions associated with hyperplasia
- Obesity
- Menopause
- Polycystic ovarian disease
- Granulosa cell tumors
- Excessive cortical function (cortical stromal hyperplasia)
- Prolonged administration of estrogenic substances.

Types of Endometrial Hyperplasia
- Simple hyperplasia without atypia
- Simple hyperplasia with atypia
- Complex hyperplasia without atypia
- Complex hyperplasia with atypia
Morphology

- **Simple hyperplasia without atypia**
  - Characterized by glands of various sizes and irregular shapes with cystic dilatation. There is a mild increase in the gland-to-stroma ratio.
  - These lesions uncommonly progress to adenocarcinoma (approximately 1%)

- **Simple hyperplasia with atypia**
  - Characterized by cytologic atypia within the glandular epithelial cells, as defined by loss of polarity, vesicular nuclei, and prominent nucleoli.
  - The cells become rounded and lose the normal perpendicular orientation to the basement membrane.
  - Approximately 8% of such lesions progress to carcinoma

- **Complex hyperplasia**
  - **Complex Hyperplasia without atypia**
    - An increase in the number and size of endometrial glands, marked gland crowding, and branching of glands. Abundant mitotic figures.
    - The glands remain distinct and nonconfluent, and the epithelial cells remain cytologically normal.
    - This class of lesions has about a 3% progression to carcinoma, lower than that of simple hyperplasia with atypia

  - **Complex hyperplasia with atypia**
    - Considerable morphologic overlap with well-differentiated endometrioid adenocarcinoma.
    - Currently, complex hyperplasia with atypia is managed by hysterectomy or, in young women, a trial of progestin therapy and close follow-up. The low rate of regression usually requires the removal of the uterus.
Thank you