CASE 4- Toy et al. CASE FILES: Obstetrics & Gynecology

A 49-year-old woman complains of irregular menses over the past 6 months, feelings of inadequacy, vaginal dryness, difficulty sleeping, and episodes of warmth and sweating at night. On examination, her BP is 120/68, heart rate is 90/min, and temperature is 99°F. Her thyroid gland is normal to palpation. The cardiac and lung examinations are unremarkable. The breasts are symmetric, without masses or discharge. Examination of the external genitalia does not reveal any masses.

What is the most likely diagnosis?

What is your next diagnostic step?
ANSWERS TO CASE 4: Perimenopause

Summary: A 49-year-old woman complains of irregular menses, feelings of inadequacy, sleeplessness, and episodes of warmth and sweating.

- **Most likely diagnosis:** Climacteric (perimenopausal state).

- **Next diagnostic step:** Serum follicle stimulating hormone (FSH) and luteinizing hormone (LH).

**Analysis**

**Objectives**

1. Understand the normal clinical presentation of women in the perimenopausal state.
2. Understand that elevated serum FSH and LH levels help to confirm the diagnosis.
3. Know that estrogen replacement therapy is usually effective in treating the hot flushes.
4. Know the risks of continuous estrogen-progestin therapy.

**Considerations**

This 49-year-old woman complains of irregular menses, feelings of inadequacy, and intermittent sensations of warmth and sweating. This constellation of symptoms is consistent with the perimenopause, or climacteric. Between the age of 40 and 51 years, the majority of women begin to experience symptoms of hypoestrogenemia, primarily hot flushes. Hot flushes, which are the typical vasomotor change due to decreased estrogen levels, are associated with skin temperature elevation and sweating lasting for 2 to 4 min. The low estrogen concentration also has an effect on the vagina by decreasing the epithelial thickness, leading to atrophy and dryness. Elevated serum FSH and LH levels are helpful in confirming the diagnosis of the perimenopause. Treatment for hot flushes includes estrogen replacement therapy with progestin.
When a woman still has her uterus, the addition of progestin to estrogen replacement is important in preventing endometrial cancer.

Note: The selective estrogen receptor modulator (SERM), raloxifene, does not treat hot flushes.

APPROACH TO THE MENOPAUSE

Definitions

Menopause: The point in time in a woman’s life when there is cessation of menses due to follicular atresia occurring after age 40 years (mean age 51 years).

Perimenopause (climacteric): The transitional 2 to 4 yr spanning from immediately before to immediately after the menopause.

Hot flushes: Irregular unpredictable episodes of increased skin temperature and sweating lasting about 3 to 4 min.

Premature ovarian failure: The cessation of ovarian function due to atresia of follicles prior to age 40 years. At ages younger than 30 years, autoimmune diseases or karyotypic abnormalities should be considered.

Physiology

At about 47 years of age, most women experience perimenopausal symptoms due to the ovaries’ impending failure. Symptoms include irregular menses due to anovulatory cycles; vasomotor symptoms, such as hot flushes; and decreased estrogen and androgen levels. Because ovarian inhibin levels are decreased, FSH levels rise even before estradiol levels fall. The decreased estradiol concentrations lead to vaginal atrophy, bone loss, and vasomotor symptoms. While most clinicians agree that estrogen replacement therapy is currently the best treatment for the vasomotor symptoms and to prevent osteoporosis, recent published data raises concerns about the risks of this therapy. The Women’s Health Initiative Study of continuous estrogen-progestin treatment reported a small but significant increased risk of breast cancer, heart disease, pulmonary embolism, and stroke. Women on hormone replacement therapy had fewer fractures and a lower incidence of colon cancer.
It should be noted that there is no evidence of adverse effects from short-term (<6mo) of estrogen therapy for the acute relief of menopausal symptoms. For women who cannot or choose not to take estrogen the antihypertensive agent clonidine may help with the vasomotor symptoms. A selective estrogen receptor modulator (SERM), such as raloxifene, is helpful in preventing bone loss, but does not alter the hot flushes. **Weight-bearing exercise, calcium and vitamin D supplementation, and estrogen replacement are important cornerstones in maintaining bone mass.** Because the FSH responds to the inhibin and not to estrogen, the FSH level cannot be used to **titrate** the estrogen replacement dose. In other words, the FSH concentration is still elevated even though the estrogen replacement may be sufficient.

Other diseases that are important to consider in the perimenopausal woman include hypothyroidism, diabetes mellitus, hypertension, and breast cancer. Women in this stage of life may also experience depression, whether spontaneous in its onset or situational due to grief or midlife adjustments. The practitioner should advocate aerobic exercise at least three times a week, again, with weight-bearing exercise being advantageous for the prevention of osteoporosis. Bone mineral density (BMD) testing, such as by dual-energy x-ray absorptiometry (DEXA), is useful in the early identification of osteoporosis and osteopenia. BMD testing is indicated for all postmenopausal women aged 65 years or older, and postmenopausal women at risk for osteoporosis and presenting with a bone fracture. Alcohol abuse may be seen in up to 10% of postmenopausal women, and requires clinical suspicion to establish the diagnosis.

**Comprehension Questions**

Match the following single best mechanism (A–H) to each of the clinical situations described (4.1–4.6). Each answer may be used once, more than once, or not at all.

- A. Gonadotropin receptor insensitivity
- B. Pituitary dysfunction
- C. Ovarian failure
- D. Ovarian cortical atrophy syndrome
- E. Peritoneal interference with ovulation
F. Hypothalamic dysfunction
G. Estrogen excess
H. Immune down-regulation of ovary


[4.2] A 22-year-old nonpregnant woman with galactorrhea and hyperprolactinemia.

[4.3] A 25-year-old woman slightly obese, slightly hirsute, and with a long history of irregular menses.

[4.4] An 18-year-old female with infantile breast development has not started her menses. She has some webbing of the neck region.


[4.6] A 33-year-old woman who has not started her menses since a vaginal delivery 1 year previously complicated by postpartum hemorrhage. She was unable to breastfeed.

Answers

[4.1] C. Ovarian failure due to follicular atresia is the reason for oligovulation in the perimenopausal years.

[4.2] F. Both hypothyroidism and hyperprolactinemia may cause hypothalamic dysfunction, which inhibits gonadotropin-releasing hormone pulsations, which in turn inhibit pituitary FSH and LH release. The lack of gonadotropins leads to hypoestrogenic amenorrhea.

[4.3] G. In polycystic ovarian syndrome, women are often obese and hirsute, have anovulation and insulin resistance, but an estrogen excess. Progestin given to these women will induce vaginal bleeding.
C. Ovarian failure is the most likely etiology in this female with probable Turner’s syndrome (45,X). It would be reflected by elevated gonadotropin levels, and streaked ovaries.

F. Excessive exercise causes hypothalamic dysfunction.

B. Sheehan’s syndrome is anterior pituitary hemorrhagic necrosis associated with postpartum hemorrhage.

CLINICAL PEARLS

- Hot flushes and irregular menses after the age of 45 years are most likely due to the climacteric, and the symptoms usually respond to estrogen replacement therapy.
- The most common location of an osteoporosis-associated fracture is the thoracic spine as a compression fracture.
- Weight-bearing exercise, calcium and vitamin D supplementation, and estrogen replacement therapy are the important cornerstones in the prevention of osteoporosis.
- Progestin should be added to estrogen replacement therapy when a woman has her uterus, to prevent endometrial cancer.
- Continuous estrogen-progestin therapy may be associated with a small but significant risk of cardiovascular disease and breast cancer.

REFERENCES


