

UNIT 4: REPRODUCTIVE ENDOCRINOLOGY, INFERTILITY & RELATED TOPICS

Educational Topic 43: Amenorrhea

Rationale: The absence of menstrual bleeding may represent an anatomic or endocrine etiology. A systematic approach to the evaluation of amenorrhea will aid in the diagnosis and treatment of its cause.

Intended Learning Outcomes:

A student should be able to:

- Define amenorrhea and oligomenorrhea
- Explain the pathophysiology and identify the etiologies of amenorrhea and oligomenorrhea, including possible nutritional causes
- Describe associated symptoms and physical examination findings of amenorrhea
- Discuss the steps in the evaluation and initial management of amenorrhea and oligomenorrhea
- Describe the consequences of untreated amenorrhea and oligomenorrhea

TEACHING CASE

CASE: A 26 year-old G2P2 woman presents to your office because she has had no periods for 9 months. She delivered two full-term healthy children vaginally and their ages are 5 and 3. She breastfed her youngest child for one year. Her menses resumed soon after weaning and were normal in duration and interval until 9 months ago. She is not using any contraception, although intercourse is infrequent. She feels very fatigued, has frequent headaches and has had trouble losing weight. She has no history of abnormal Pap smears or STI's. She takes no medications. She is married and works from home as a computer consultant. On exam, BP= 120/80, P= 64, Ht= 5'8", Wt= 160 pounds. She appears tired but in no distress. Breast exam reveals no masses, dimpling, galactorrhea or retraction. Pelvic exam shows dry vaginal mucosa but is otherwise normal. HCG is negative.

COMPETENCY-BASED DISCUSSION & KEY TEACHING POINTS:

Competencies addressed:

- Patient care
- Medical Knowledge
- System-Based Practice

1. Does this patient have primary amenorrhea, secondary amenorrhea or oligomenorrhea?
 - Primary amenorrhea definition: age 14 without secondary sex characteristics, age 16 with secondary sex characteristics
 - Secondary amenorrhea definition: 6 months of amenorrhea after a history of normal menses
 - Oligomenorrhea: menstrual interval >35 days but less than 6 months
2. What is the differential diagnosis for this disorder? Describe the relevant associated symptoms, physical exam findings, laboratory findings and pathophysiology for each of these.

Differential diagnosis for secondary amenorrhea:

- Pregnancy
 - Hypothalamic---Pituitary Dysfunction
 - Prolactin excess
 - About 1/3 have no symptoms; 2/3 have galactorrhea
 - Pituitary adenoma
 - Hypothyroidism: extremely elevated TSH may cause prolactin to rise
 - Medications: phenothiazines, antidepressants, antihypertensives, metoclopramide, all can cause elevated prolactin, narcotics, estrogens, marijuana
 - Function/psychogenic: Etiologies include weight loss, excessive exercise, psychologic stress, chronic illness related stress, brain or head injury, anorexia nervosa
 - Neoplastic: brain tumor
 - Ovarian Dysfunction
 - Premature ovarian failure: cessation of menses age < 40, testing for fragile X, associated with elevated FSH
 - Other: From radiation or chemotherapy exposure
 - Genital Outflow Tract Abnormalities, specifically Asherman's syndrome, usually associated with uterine procedures like D&C
 - Anovulation is commonly associated with oligomenorrhea but can present with amenorrhea as well
 - Polycystic ovarian syndrome:
 - Thyroid dysfunction
3. What additional studies are needed?
 - Prolactin 12 ng/ml (normal range <22) & TSH 1.2 uIU/ml (normal range: 0.4-4.0)
 - Progesterone challenge is negative consistent with hypogonadism. Progesterone challenge can distinguish anovulation versus a pituitary or hypothalamic etiology. Bleeding after progesterone challenge establishes a patient outflow tract and competent endometrium that has been thickened by endogenous estrogen.
 - Next step in hypogonadism is FSH 80 uIU/ml. This establishes the diagnosis of hypergonadotropic hypogonadism consistent with premature ovarian insufficiency (POI)
 - In addition to evaluation for POI replace estrogen in order to protect against osteoporosis (and progestin to protect the uterus).

4. Consider that this patient has a prolactin level of 130. The test, when repeated with the patient fasting is 100. What is your next step?
 - Pituitary MRI
 - Treat with dopamine agonist like bromocriptine

5. How would your next step differ if the patient had normal labs with an estradiol level of 30pcg/ml and an FSH of 2mIU/ml. What further evaluation is needed and what treatment would you offer her? What is she at risk for?
 - Hypogonadotropic hypogonadism
 - Next step in management is an MRI of the head. In this case, the MRI is considered normal implying hypothalamic amenorrhea. Further questions regarding her exercise and eating habits is warranted.
 - Replace estrogen in order to protect against osteoporosis

6. If the patient had a withdraw bleed to a progestational challenge and a normal TSH and prolactin, what would be the most likely diagnosis, first line treatment, and long term concern if untreated?
 - Polycystic ovarian syndrome
 - If not wanting to conceive, combined contraceptives are best first line treatment. If wanting to conceive, ovulation induction with clomiphene citrate.
 - Long term the patient is at risk for endometrial hyperplasia / uterine cancer if not treated with progestins regularly. Patient is also at increased risk of diabetes and high cholesterol.

REFERENCES

Beckman CRB, et al. Obstetrics and Gynecology. 7th ed. Philadelphia: Lippincott, Williams & Wilkins, 2013.

Hacker NF, Moore JG, et al. Essentials of Obstetrics and Gynecology. 5th ed. Philadelphia: Saunders, 2010.