

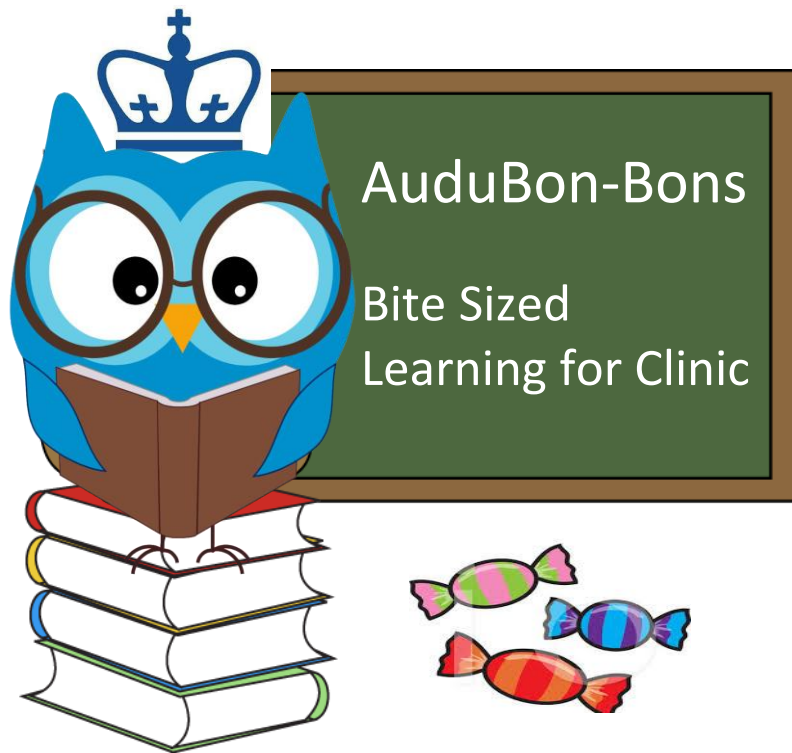
SECONDARY AMENORRHEA

Week 24

Prepared by Henry James Behar, MD

Reading Assignment:

CREOGs Over Coffee podcast Episode 2: Diagnosis and Workup of Secondary Amenorrhea (October 7, 2018)



LEARNING OBJECTIVES

- To determine the most common causes of secondary amenorrhea
- To determine the best management options for secondary amenorrhea



CASE VIGNETTE

- A 28yo G0 woman with LMP “4 months ago” presents to 21 Audubon concerned that she has not had her period in a long time.
- She states that she has taken home pregnancy tests and they are all negative.
- Patient reports that she had previously experienced regular monthly menstruation.



DEFINITION

- What is the definition of secondary amenorrhea?
 - The cessation of previously regular menses for three months or previously irregular menses for six months



FOCUSED HISTORY

- What elements of the patient's history are most important?
 - PMH: denies
 - PSH: denies
 - PObH: nulligravida
 - PGynH: denies history of STIs, fibroids, cysts or abnormal Paps
 - Meds: multivitamins Allergies: NKDA
- Important questions to ask:
 - Recent weight loss? Change in exercise routine? Stress?
 - Review medications, including contraception
 - Constitutional sx? Unwanted hair growth? Acne?
 - Headaches? Galactorrhea?
 - Hot flashes, vaginal dryness, poor sleep, or decreased libido?
 - History of PPH, severe bleeding, dilatation and curettage, endometritis or other infection?



PERTINENT PHYSICAL EXAM FINDINGS

- Vital signs: HR 94, BP 104/68, T 98.4, RR 12, Ht 170cm, Wt 50.1kg
- Breast: Tanner stage 5, no masses or lesions noted
- External Genitalia: Tanner stage 5, grossly normal
- Vagina: no bleeding or discharge noted
- Cervix: nulliparous, no visible lesions
- Uterus: small, firm and mobile with normal contour
- Adnexa: no palpable masses, nontender bilaterally

- Important to note:
 - BMI
 - Secondary sexual characteristics; Tanner stage
 - Evidence of hirsutism? Acne? Acanthosis nigricans?
 - Galactorrhea?
 - Signs of hypoestrogenism?
 - Erosion of dental enamel?



DIFFERENTIAL DIAGNOSIS

- Pregnancy
- Hypothalamic (functional hypothalamic amenorrhea)
 - Weight loss, Exercise, Stress
 - Systemic illness severe enough to result in a decrease in hypothalamic GnRH secretion and/or associated with nutritional deficiencies (Type 1DM, celiac disease)
- Pituitary
 - Hyperprolactinemia
 - Other sellar mass (craniopharyngiomas, meningiomas)
 - Sheehan syndrome, radiation, infarction, infiltrative lesions of pituitary, such as hemochromatosis
- Thyroid disease – hypo or hyper
- PCOS
 - Other hyperandrogenic conditions, classic or nonclassic 21-hydroxylase deficiency
- Ovary
 - Primary ovarian insufficiency (very rarely Turner syndrome)
 - Ovarian androgen-secreting tumor
- Outflow Tract
 - Asherman syndrome
 - Cervical stenosis

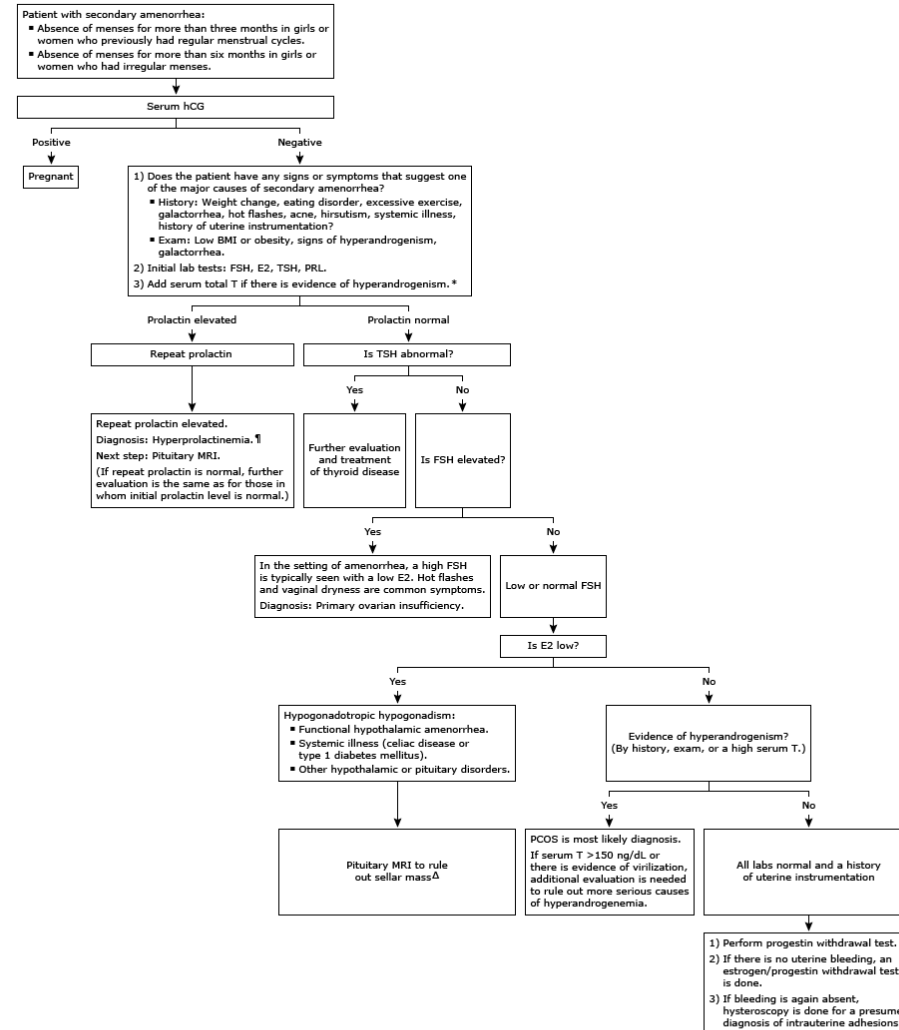


EVALUATION

- History
- Physical Examination
- Initial Serology
 - β HCG
 - Prolactin
 - TSH, reflex fT4
 - FSH if suggested by history
- If evidence of hyperandrogenism --> Testosterone, DHEAS
- Progestin withdrawal test to assess estrogen status
 - medroxyprogesterone 10 mg for 10 days
 - withdrawal bleeding confirms that there has been endogenous estrogen exposure
 - Absence of bleeding can be due to either hypoestrogenism or an outflow tract disorder
- PUS, bone mineral density, if suggested by history



Evaluation of secondary amenorrhea



This algorithm offers a stepwise approach to the evaluation of secondary amenorrhea. For further details, refer to additional content on the causes, evaluation, and treatment of secondary amenorrhea.

hCG: human chorionic gonadotropin; BMI: body mass index; FSH: follicle-stimulating hormone; E2: estradiol; TSH: thyroid-stimulating hormone; PRL: prolactin; T: testosterone; MRI: magnetic resonance imaging; PCOS: polycystic ovary syndrome.

* Many clinicians also measure serum 17-hydroxyprogesterone at the initial visit to rule out nondiagnostic 21-hydroxylase deficiency. Some also measure serum dehydroepiandrosterone sulfate (DHEAS).

† Mild hyperprolactinemia can sometimes be seen with hypothyroidism. Euthyroidism should be confirmed before performing MRI.

Δ Pituitary MRI not required in those with clear explanation for their hypogonadotropic amenorrhea, eg, eating disorder, excessive exercise, celiac disease, or type 1 diabetes mellitus.



PATHOPHYSIOLOGY

- Hypothalamic Amenorrhea
 - Unclear
 - Associated with decreased caloric intake, increased exercise, increased stress
 - “Athletes Triad”
 - Disruption of normal pulsatile hypothalamic gonadotropin-releasing hormone secretion
 - Absent midcycle luteinizing hormone surge
 - Lack of ovarian follicular development
 - Anovulation
 - Low serum estradiol concentrations



MANAGEMENT

- Hypothalamic amenorrhea
 - Lifestyle changes
 - Nutritional counseling
 - Multidisciplinary team specializing in treatment of eating disorders
 - Low bone density
 - Cognitive behavioral therapy
- Hyperprolactinemia
 - Depends on cause
 - Fertility?
- Primary ovarian insufficiency (premature ovarian failure)
 - Estrogen therapy for prevention of bone loss
- Intrauterine adhesions
 - Hysteroscopic lysis of adhesions followed by estrogen treatment to stimulate regrowth of endometrium
- Polycystic ovary syndrome
 - Relief of hirsutism, resumption of menses, fertility
 - Prevention of long-term consequences of PCOS, such as endometrial hyperplasia, obesity, and metabolic disorders
 - Fertility?
- Thyroid disease



SOCIAL DETERMINANTS OF HEALTH

Functional hypothalamic amenorrhea is underlying cause of up to 35% of women seeking evaluation for secondary amenorrhea.

- Most commonly observed in women athletes and those with clinical and sub-clinical eating disorders (both over and under-eating)
- Due to stress-induced suppression of endogenous GnRH leading to elevated cortisol.

Stress and obesity can act synergistically to increase inflammation and lead to brain aging and other conditions of neurodegeneration!

Secondary amenorrhea resulting from FHA should be used as an early warning sign to intervene to decrease burden of stress.

- Essential for both fertility preservation and overall brain cell health



EPIC .PHRASE

.BBonSecondaryAmenorrhea

Description: Secondary Amenorrhea

The patient was counseled about secondary amenorrhea, or the absence of menses for 3 months in the setting of previously normal menses or 6 months with previously irregular menses. A pregnancy test was performed which was ***. Initial laboratory studies were sent including TSH, PRL, E2, and FSH. Further management will be undertaken based on initial results.



CODING AND BILLING

- ICD-10: N91.1 – Secondary Amenorrhea
- CPT Code 99213 requires at least 2 of following 3 items:
 - Expanded problem focused history (CC, brief HPI, pertinent ROS)
 - Expanded problem focused exam (Limited to affected body region/organ)
 - Medical decision-making of low complexity



EVIDENCE

- References

- [ASRM Practice Committee: Current Evaluation of Amenorrhea](#)
- [ASRM Grand Rounds: Amenorrhea](#)
- [Female athlete triad. Committee Opinion No. 702. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;129:e160–7](#)
- [Premature Ovarian Failure Rebar, RW Obstetrics & Gynecology: June 2009 - Volume 113 - Issue 6 - p 1355-1363](#)
- [Amenorrhea: an approach to diagnosis and management. David A. Klein, Merrily A. Poth Am Fam Physician. 2013 Jun 1; 87\(11\): 781–788.](#)
- Evaluation and management of secondary amenorrhea, UpToDate
- Epidemiology and causes of secondary amenorrhea, UpToDate
- Prokai D, Berga SL. Neuroprotection via Reduction in Stress: Altered Menstrual Patterns as a Marker for Stress and Implications for Long-Term Neurologic Health in Women. Int J Mol Sci. 2016. Dec; 17(12): 2147.

