CASE TWO

Short case number: 3_24_2
Category: Endocrine and Reproductive Systems
Discipline: Obstetrics & Gynaecology
Setting: General Practice
Topic: Secondary Amenorrhoea

Case

Rhonda Birchgrove is a 24 year old competitive marathon runner who is seeking advice about the irregularity of her menstrual cycle. In fact, she tells you that she has not had a period for 4 months (not that she is complaining as it interferes with training) but she felt she should get some advice to tell her it is normal. Her home pregnancy test is negative.

Questions

1. What is the standard length of time of amenorrhoea that is used for classification purposes? By definition, what functions must a woman's reproductive system have to undergo secondary amenorrhoea?
2. List from 'head to toe', the classification system for secondary amenorrhoea as well as the relative frequencies of these processes.
3. Discuss how increased levels of prolactin can cause secondary amenorrhoea and the major treatments for hyperprolactinaemia.
4. Discuss the major hypothalamic causes of secondary amenorrhoea including weight loss, exercise and psychological stress.
5. Discuss the most significant effects to the woman of prolonged amenorrhoea

Suggested Reading

- Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier
- Dewhurst's Textbook of Obstetrics & Gynaecology, Edmonds K [editor]. Blackwell Publishing. 2007. Chapter 39 – pg 389-396

Define Secondary Amenorrhoea:

- 6 consecutive months of no menstruation
- in woman who has previously had regular periods

What functions must a woman's reproductive system have to undergo secondary amenorrhoea.

- Patent lower genital tract
- Endometrium that responds to ovarian hormone stimulation
- Ovaries that respond to pituitary gonadotrophins

Causes / Classification of Secondary Amenorrhoea?

PATCHES
PCOS, Pregnancy
Asherman, norexia
Thyroid Disease
Cushing's
Hyperprolactinoma
Excercise
Stress (Chronic Ilness or Psychological)

UTERINE

- Asherman's syndrome (Adhesions in Uterus after surg)
- Cervical Stenosis (narrowing of cervic in pre-menopausal women prevents blood exiting cervix)

OVARIAN

- PCOS
- Premature Ovarian Failure

HYPOTHALAMIC

- Weight Loss
- Excercise
- Stress (Illness / Psych)

PITUITARY

- Hyperprolactinaemia
- Hypopituitarism

TRAUMA TO HYPOTHALAMUS / PITUITARY

ENDOCRINE

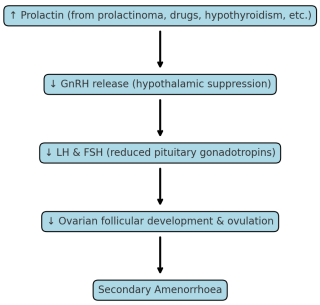
- Thyroid
- Cushings

PROLACTIN
How do elevated levels of prolactin cause secondary amenorrhoea.

1. Hyperprolactinaemia caused by:
    a. Prolactinoma (on pituitary)
    b. Non-functioning hypothalamic-Pituitary tumour - *Disconnects communication between the two*
    c. *PCOS*

d. *Iatrogenic (Anti-psychotics, anti-emetics)*
e. *Stress, Anxiety, Sleep Deprivation*

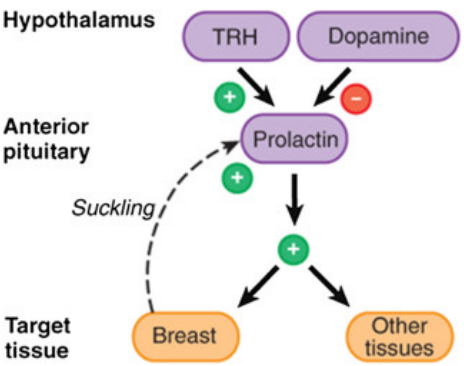
2. High prolactin suppresses GnRH → ↓ LH/FSH → no follicular maturation or ovulation → secondary amenorrhoea.

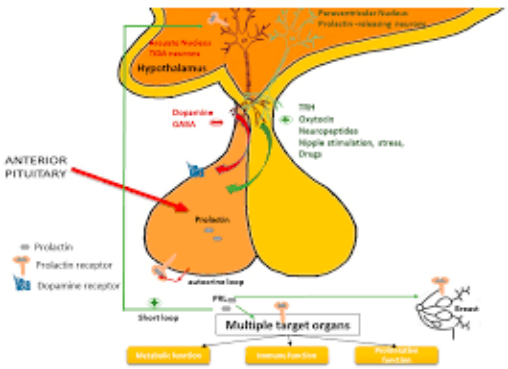


What are the main treatment for hyperprolacinaemia?

- Dopamine Agonist (cabergoline or bromocriptine)
- Surgical Resection of adenomas

DOPAMINE HAS INHIBITORY EFFECT ON PROLACTIN





HYPOTHALAMIC CAUSES OF SECONDARY AMENORRHOEA

What are the major hypothalamic causes of secondary amenorrhoea?

Weight Loss - *Fat appears to be fundemental in maintaining normal HPA function (BMI<19 causes amenorrhoea)*

Excessive Exercise *- Assoc with low fat levels (same mech as weight loss)*

Psychological Stress - *The stress itself does not cause, it is thought that caused by weight loss that accompanies stress*

These all work by reducing GnRH pulsatility, leading to hypogonadotropic hypogonadism
(↓GnRH Pulsatility =↓ LH/FSH → anovulation → amenorrhoea)

What affects does prolonged amenorrhoeah have on a woman:

- Anovulation --> Infertility
- If HPA or ovarian cause = Low Estrogen --> Osteopenia/perosis, Vaginal Dryness, Estrogen normally cardioprotective

- Hyperprolactinaemia cause -->Galactorrhea, headaches, visual

ANSWERS

Question 1

Cessation of menstruation for 6 consecutive months in a woman, who has previously had regular periods, is the usual definition for secondary amenorrhoea. However, some authorities consider 3 or 4 months of amenorrhoea to be pathological but here we enter the grey area between amenorrhoea and oligomenorrhea. Women with secondary amenorrhoea must have a patent lower genital tract, an endometrium that is responsive to ovarian hormone stimulation and ovaries that have responded to pituitary gonadotropins.

Question 2

Classification of secondary amenorrhoea

Uterine causes
- Asherman's syndrome
- Cervical stenosis

Ovarian causes
- Polycystic ovarian failure
- Premature ovarian failure (genetic, autoimmune, infective)

Hypothalamic causes
- Weight loss
- Exercise
- Chronic illness
- Psychological distress
- Idiopathic

Pituitary causes
- Hyperprolactinemia
- Hypopituitarism

Hypothalamic/pituitary damage
- Cranial irradiation
- Head injury
- Tumours
- Sarcoidosis

Systemic causes
- Chronic debilitating illness
- Weight loss
- Endocrine disorders (thyroid, Cushings syndrome)

Question 3

Hyperprolactinaemia is the commonest pituitary cause of amenorrhoea. There are many causes of a mildly elevated serum prolactin concentration, including stress and a recent physical or breast examination. If the prolactin concentration is greater that 1000mu/l then the test should be repeated and the sample checked for macroprolactin (PEG separation test). Elevated levels of macroprolactin are of no clinical significance, and will be interpreted as hyperprolactinaemia if a PEG separation test is not done. If true hyperprolactinaemia, it is necessary to image the pituitary fossa (as well as checking for a history of headaches, visual disturbances, galactorrhoea etc, and examination of visual fields).

Hyperprolactinaemia may result from a prolactin secreting pituitary adenoma, or from a non functioning disconnection tumour in the region of the hypothalamus or pituitary which disrupts the inhibitory influence of dopamine on prolactin secretion. Other causes of hyperprolactinaemia include PCOS and several drugs (anti psychotics, anti emetics: domperidone, metoclopramide, methyl dopa, OC pill). Stress, anxiety and sleep deprivation can also cause elevated prolactin.

Medical management of hyperprolactinaemia (and pituitary microadenoma) is a dopamine agonist (cabergoline or bromocriptine). The main side effect of these drugs is hypotension. Cabergoline is administered as a dose once a week, and is the drug of choice. Macroadenomas may need surgical (transphenoidal) resection. Potential side effects include CSF leak, infection and incomplete removal of tumour. Medical management will shrink most macroadenomas so surgery rarely indicated.

Question 4

Weight related amenorrhoea.

Weight can have profound effects on gonadotropin regulation and release. Weight and eating disorders are common in men and women. A regular menstrual cycle will not occur if the BMI is less than 19kg/m2. Fat appears to be critical to a normally functioning hypothalamic pituitary gonadal axis.

Physiological stress.

Studies have failed to demonstrate a link between stressful life events and amenorrhoea of greater than 2 months. However, stress may lead to physical debility such as weight loss which may then cause menstrual disturbance.

Exercise-related amenorrhoea.

Menstrual disturbance is common in athletes undergoing intensive training. Between 10 – 20 % have oligomenorrhea compared with 5% of the normal population. The main aetiological factors are weight and percentage body fat content.