Secondary amenorrhoea
Dr. ASMAA AL SANJARY

The student at the end of this lecture should be able to:

Define secondary amenorrhoea.
Classify the causes of secondary amenorrhoea.
Describe the commonest three cases of secondary amenorrhoea.
Analyze the history and examination of a case of secondary amenorrhoea.
Diagram an outline of a case of secondary amenorrhoea.
Analyze the diagnostic role of progesterone challenge test.

Secondary amenorrhoea is cessation of menstruation for 6 consecutive months in a woman who has previously had regular periods or for 12 months in a woman with previous oligomenorrhoea.

**WOMEN WITH SECONDARY AMENORRHOEA**

- Must have a patent lower genital tract.
- Endometrium that have responsive to hormonal stimulation.
- Ovaries that have responded to pituitary gonadotrophin.

-Amenorrhoea is absence of menstruation, which might be temporary or permanent.

-It may occur as normal physiological condition as before puberty, during pregnancy, lactation, or after menopause.
OR as a feature of a systemic or endocrine disease

CLASSIFICATION OF SECONDARY AMENORRHOEA

UTERINE CAUSES

- Asherman’s syndrome
- Cervical stenosis: after cone biopsy (require dilatation)

OVARIAN CAUSES

- PCOS
- Premature ovarian failure: genetic, autoimmune, infective, radio/chemotherapy.

HYPOTHALAMIC CAUSES

(HYPOGONADOTROPHIC HYPOGONADISM)

- Weight loss
- Exercise
- Chronic illness
- Psychological distress
- Ideopathic

PITUITARY CAUSES

- Hyperprolactinaemia
- Hypopitutarism (Sheehan’s syndrome)

CAUSES OF HYPOTHALAMIC/PITUITARY DAMAGE (HYPOGONADISM)

- Tumors (craniopharyngiomas, gliomas, germinomas, dermoid cysts)
- Cranial irradiation
• Head injuries
• Tuberculosis
• Sarcoidosis

SYSTEMIC CAUSES
• Debilitating illness
• Endocrine disorders (thyroid disease, cushing syndrome,..)
• Drugs: COCP, danazol

THE MOST COMMON CAUSES OF SECONDARY AMENORRHOEA

• POLYCYSTIC OVARY SYNDROME
• PREMATURE OVARIAN FAILURE
• HYPERPROLACTINAEMIA

THESE ACCOUNTS FOR 75 % OF CASES

MANAGEMENT OF A CASE OF SECONDARY AMENORRHOEA

HISTORY AND EXAMINATION:
- Any change in weight (BMI between 20-25 kg/m²)
- Unusual exercise or stress
- Intrauterine instrumentation (pregnancy termination)
- Drug history
- Family history of premature menopause
- signs of hyperandrogenism or virilism.
- signs of hyperthyroidism or hypothyroidism
- signs of cushing’s syndrome
- bitemporal hemianopia and visual disturbance
- examination of the breast for galactorrhoea
- bimanual pelvic examination.

*Always exclude pregnancy in a women of any age in case of secondary amenorrhoea.*

**Endocrine Investigation:**

- Baseline gonadotrophin level (FSH,LH)
  
  FSH and LH > 15 IU/l indicate impending ovarian failure (unrelated to preovulatory surge), their level can differentiate ovarian from hypothalamic causes. LH raise alone will indicate PCOS
  
  - Serum prolactin
  
  if > 1500 mIU/l indicate pituitary microadenoma.
  
  - Thyroid function test

- Oestrogen state of the endometrium: by examination of the genital tract or induce withdrawal bleeding by progesterone administration.
• Serum testosterone: if greater than 5 nmol/l should be investigated to exclude adrenal or ovarian tumors.

• 24 hour urinary cortisol: is elevated in cushing syndrome(700 nmol/24 hr).

Other investigation like:

• Ultrasound : to exclude PCOS, ovarian cyst or tumor, post menstrual endometrial thickness if >10mm then endometrial biopsy indicated to exclude malignancy.
• Hystyrosalpingography and hysteroscopy: in cases suspected to have asherman’s syndrome.
• CT scan or MRI : hypothalamic tumor, non functioning pituitary tumor compressing the hypothalamus or a prolactinoma.

• Skull X ray
• Karyotype: in patient of premature ovarian failure(<40 years) to exclude sex chromosomes mosaisim.
• Auto antibody screen: in patient with POF.
management of individual causes

Asherman’s syndrome:

Is a condition in which intauteine adhesions prevent normal growth of the endometrium.

Aetiology:

1. Too vigorous endometrial curettage affecting the basalis layer of the endometrium.
2. Episodes of endometritis.
3. Oestrogen deficiency in breast feeding

Women

Amenorrhoea is not absolute, withdrawal
Bleeding can be induced with oestrogen /progesterone administration.

Diagnosis: by HSG and or hysteroscopy.

Treatment: by adhesiolysis followed by 3 months of oestrogen progesterone cyclical therapy. A foley catheter can be inserted postoperatively for 7-10 days, or IUD
inserted for 2-3 months.

The pregnancy rate after treatment depends on initial severity of the adhesions
- 93% for mild adhesions
- 57% for severe adhesions

**Premature ovarian failure (POF)**
Is cessation of periods accompanied by raised gonadotrophin level prior to the age of 40 years.
It occurs in 1-5% of female population.

POF have increased risk of:
- osteoporosis
- cardiovascular disease

**Aetiology:**
1. Chromosomal abnormality: it occurs in 70% of cases of primary amenorrhea
2. % of cases of secondary amenorrhea
3. Autoimmune disease.
5. Surgery.
Treatment:

**oestrogen deficiency** : HRT preparation

**Infertility**: in established cases there is resistant to gonadotrophin with absence of ovarian follicle, and reports of pregnancy in treated cases only indicate fluctuating ovarian function rather than treatment success.

---

Hyperprolactinaemia:

Is the commonest pituitary cause of secondary amenorrhoea.

Causes of elevation of serum prolactin:

**Mild elevation**: - pregnancy (10 fold)
- stress.
- venepuncture.
- postprandial.
- breast examination.

**Moderate elevation**:
- hypothyroidism
- PCOS (up to 2500 IU/l)
- drugs: dopaminergic antagonist phenothiazines, domperidone, verapamil, methyldopa, metoclopramide and oestrogen.

**Sever elevation**:
- prolactin secreting tumor: micro and macroadenoma.
- non-functioning tumor of the hypothalamus or pituitary

Symptoms of hyperprolactinaemia:
• Amenorhoea: is the bioassay of prolactin excess.
• Galactorrhoea: in up to 1/3 of patients.
• Symptoms of hypooestrogenism (amenorrhoea no withdrawal bleeding after progesterone therapy)
• Visual disturbances. (bitemporal hemianopia)

Diagnosis:
• Prolactin serum assay: (tumor marker)
• Skull X ray:
  - asymmetrical enlarged pituitary fossa with double contour of it’s floor.
  - Erosion of the clinoid processes.
• Ct-scan or MRI

Treatment of galactorrhea and amenorrhoea

Observation:
• periodic observation for patient with galactorrhea who have normal prolactin or idiopathic elevation.
• Patient with oligomenorrhea who not desire fertility should be treated with periodic progesterone if not desire fertility and with COCP, if contraception is required. Failure of progestin to introduce bleeding is suggestive of hypooestrogenism.

• Long term treatment with bromocriptine in women with normal estrogen is not indicated.
• Observation can be extended to some women with radiologic evidence of pituitary microadenoma (<=10mm in diameter) because the growth rate is slow, an annual measurement of serum prolactin is appropriate in patient with normal oestrogen level.
• Macroadenoma >=10mm require further evaluation by periodic scanning and possible treatment.

Medical treatment:
• Patient aim to restore menstrual cyclicity or to prevent osteoporosis COCP are given.
• Patient require reduction of prolactin and restoration of cyclic physiologic estrogen secretion require ergot compund:

• Bromocriptine:dopamine antagonist: starting with small dose of 1.25 mg at bed time increased gradually 7.5 mg in divided Daily doses to initiate response then reduce To a maintenance lower dose .some tolerate the drug more if given vaginally. Side effect :nausea,vomiting,headache• postural hypotension

• Cabergoline :longer acting ,better tolerated,more expensive Given in 0.25 mg twice weekly•

✓ Bromocriptine normalizes the secretion of prolactin in 82% of cases of women with microadenoma and restore cycle and fertility in more than 90%. It require 6-10 weeks to restore cycle and 10-16week to establish ovulation. discontinuation of therapy result into return of hyper-prolactinaemia leading to galactorrhea and amenorrhea.

✓ Patient with macroadenoma require visual field assesment,other pituitary hormone assesment,repeat MRI after full therapeutic dose of bromocriptine is reached.treatment is continued as long as shrinkage of adenoma is required

✓ During pregnancy treatment is stopped tumors unlikely to enlarge during pregnancy,macroadenoma extending beyound the sella tursica require debulking surgery before pregnancy (15%-30%) risk of enlargement, bromcriptine therapy is started.patient require repeated visual field assessment once abnormality develops
Bromocriptine is instituted or increased for the rest of pregnancy. (there is no increase in congenital abnormality)

Medical treatment is preferred over surgery as recurrence is high: microadenoma recure 30% and macroadenoma recurs in 90%.

**Surgical : transphenoidal adenectomy**

**Indicated in cases of**

- Resistance to treatment.
- Intolerance to medical treatment.
- Supracellar extention not respond to bromocriptine and pregnancy is desired

**Radiotherapy:** is not desired with modern surgery