Problem solving - Approach to secondary amenorrhoea

Dr Marilyn Lee
KTPH
Objectives

• Causes of secondary amenorrhoea
• Evaluation
• Management
• HRT vs OCP
• Learning points
• 26/F
• Amenorrhoea 8 months
• Not sexually active
• Menarche age 13, regular until a year ago.
• History of migraines – no regular meds
• No hot flushes, vaginal dryness
• No hirsutism/acne/scalp hair loss

• BMI 20 kg/m²
• No galactorrhoea
• Clinically euthyroid
• Bp 116/74

FT4 17.5 pM, TSH 2.4 mu/L
LH 3.0 mu/L, FSH 4.2 mu/L
Testosterone – within normal limits
Prolactin – within normal limits
Definition

• Secondary amenorrhoea refers to absence of menses for over 3 months in women who previously had regular menstrual cycles, or 6 months in women who had irregular menses.
Introduction

• The menstrual cycle is susceptible to external influences, hence, missing a single period is rarely important

• In contrast, prolonged amenorrhoea may be the earliest sign of a decline in general health or signal an underlying medical problem (eg hyperthyroidism)

• Always exclude pregnancy
• HYPOTHALAMIC-PITUITARY-OVARIAN AXIS
Hypothalamic dysfunction
- Functional hypothalamic amenorrhea
- Inflammatory/infiltrative disease
- Tumour
- Traumatic brain injury
Pituitary disease
- hyperprolactinemia
- empty sella
- other sellar masses
- other diseases of the pituitary
Ovarian (PCOS, POF)  
Uterine (Asherman)
Approach – history and examination

- Hypothalamic
  - Eating disorders, high intensity exercise, stress, chronic severe illness, traumatic brain injury
- Pituitary
  - Galactorrhoea, drugs
  - Symptoms/signs of cushing’s or acromegaly
- Ovarian
  - Symptoms of oestrogen deficiency
  - Hirsutism/acne/scalp hair loss*
- Others
  - Symptoms of thyroid dysfunction
  - Virilization
  - Uterine instrumentation
Diagnostic evaluation

• Laboratory investigations
  – Gonadotropins, TFT, prolactin
  – Consider testosterone, 17OHP

• USS pelvis
  – Polycystic ovaries?
  – Endometrial thickness

• Progestin withdrawal
History and examination

- hCG, TFT, prolactin
  - abnormal
    - FSH
      - high
        - Evaluate for thyroid dysfunction, hyperprolactinemia
      - Premature ovarian insufficiency
  - Oestrogen replete
    - Combined oestrogen and progestin
      - FHA
      - Hypothalamic-pituitary
      - Anatomic defects
  - Oestrogen deplete
    - Withdrawal bleed
    - No withdrawal bleed
      - Progestin withdrawal
      - No withdrawal bleed

*additional tests if clinically indicated

Testosterone, 17OHP, ONDST
• 26/F
• Amenorrhoea 8 months
• Not sexually active
• Menarche age 13, regular until a year ago.
• History of migraines – no regular meds
• No hot flushes, vaginal dryness
• No hirsutism/acne/scalp hair loss

• BMI 20 kg/m2
• No galactorrhoea
• Clinically euthyroid
• Bp 116/74

FT4 17.5 pM, TSH 2.4 mu/L
LH 3.0 mu/L, FSH 4.2 mu/L
Testosterone – within normal limits
Prolactin – within normal limits
Question

Which of the following statements is true?

1. This is not PCOS because testosterone level is not elevated
2. A normal BMI excludes hypothalamic amenorrhoea
3. As blood tests are all normal, no further evaluation is required
4. An USS showing a thin endometrial lining makes PCOS less likely
Rotterdam Criteria

• 2 out of 3:
  – Oligo/amenorrhoea and/or anovulation
  – Hyperandrogenism
  – Polycystic ovaries on USS
PCOS – An Endocrine perspective

High LH - ~ 40% - Marker for anovulation in lean women
High Testosterone - ~ 50% - Marker for hirsutism
High Insulin - ~ 30% - Marker for oligomenorrhoea and T2DM
High AMH - ~ 70% - Marker of follicle count
• US – polycystic ovaries, endometrial thickness 3mm, ovarian volume 8ml

• Further history – runner of 15-20km at least 3 times a week
Question

What is the most likely diagnosis?
1. Polycystic ovarian syndrome
2. Functional hypothalamic amenorrhoea
3. Premature ovarian insufficiency
4. Non classic congenital adrenal hyperplasia
Normal gonadotrophin amenorrhoea

Usually PCOS or Hypothalamic Amenorrhea (HA)

<table>
<thead>
<tr>
<th></th>
<th>PCOS</th>
<th>HA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise program?</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>BMI</td>
<td>Any - usually &gt; 21</td>
<td>Usually &lt; 21</td>
</tr>
<tr>
<td>Androgen excess</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Suppressed LH</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Polycystic Ovaries</td>
<td>&gt;90%</td>
<td>20%</td>
</tr>
<tr>
<td>Endometrial thickness</td>
<td>Rare &lt; 5 mm</td>
<td>&lt; 5 mm</td>
</tr>
</tbody>
</table>
Management

• Anovulatory cycles and oestrogen replete
  – Progesterone every 2-3 months
  – Eg Dydrogesterone 10mg BD x 1 week

• Oestrogen deplete
  – Combined oestrogen and progesterone (either OCP or HRT)
Question

DEXA scan shows z score of -2.1 in both left hip and lumbar spine.
Apart from advising her to reduce exercise, how would you manage her?

1. OCP
2. HRT
3. Watch and wait
HRT vs OCP

Oestrogen  21

Progesterone  28
<table>
<thead>
<tr>
<th>Sequential oestrogen and progesterone combinations</th>
<th>Continuous combined</th>
<th>Unopposed oestrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets</td>
<td>Oestrogen</td>
<td>Progesterone</td>
</tr>
<tr>
<td>Trisequens</td>
<td>Oestrogen 1,2mg</td>
<td>Norethisterone</td>
</tr>
<tr>
<td>Progylutan</td>
<td>Oestrogen 2mg</td>
<td>Norgestrel</td>
</tr>
<tr>
<td>Femoston</td>
<td>Oestrogen 1,2mg</td>
<td>Dydrogesterone</td>
</tr>
<tr>
<td>Other oestrogens</td>
<td>Type</td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------------</td>
<td></td>
</tr>
<tr>
<td>Oestrogel</td>
<td>Oestradiol Gel</td>
<td></td>
</tr>
<tr>
<td>Divigel</td>
<td>Oestradiol Gel</td>
<td></td>
</tr>
<tr>
<td>Norethisterone</td>
<td>Norethisterone 5mg</td>
<td>Tablets</td>
</tr>
<tr>
<td>Provera</td>
<td>Medroxypregesterone 10mg</td>
<td>Tablets</td>
</tr>
<tr>
<td>Depot provera</td>
<td>Medroxypregesterone 150mg/3ml injection</td>
<td>Injection</td>
</tr>
<tr>
<td>Mirena</td>
<td>Levonorgestrel (20mcg/24hr)</td>
<td>IUS</td>
</tr>
<tr>
<td>Duphaston</td>
<td>Dydrogesterone 10mg</td>
<td>Tablets</td>
</tr>
<tr>
<td>Uterogestan</td>
<td>Micronized progesterone 100mg</td>
<td>Capsules</td>
</tr>
<tr>
<td>Progesterone injection</td>
<td>Progesterone 50mg/ml (5-10mg daily)</td>
<td>Deep im injection</td>
</tr>
</tbody>
</table>
Learning points

• Always exclude pregnancy
• Once thyroid dysfunction and hyperprolactinemia are excluded, FSH should be done to distinguish between a primary ovarian pathology vs other causes
• PCOS and HA are the commonest causes of anovulatory cycles.
• Differentiating between them may require a combination of history, examination, biochemical and radiological tests.
References


