***Secondary amenorrhea***

***د. زينب عبد الأمير جعفر***

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* ***The student will be able to list:***
  1. ***Definition of secondary amenorrhea***
  2. ***Causes of secondary amenorrhea***
  3. ***Evaluation patient with secondary amenorrhea***
  4. ***Treatment options for them***

***Definition:***

***Secondary amenorrhea****:is absence of menstruation for more than 6 months in a normal female of reproductive age who had menses previously and that is not due to pregnancy, lactation or the menopause.*

*Oligomenorrhoea :is the occurrence of five or fewer menstrual periods over 12 month*

***Prevalence****:**about 3%*

***Classification:***

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| --- | --- |
| 1. ***Synechiae (ASherman's syndrome)*** 2. ***Ablation of endometrium (eg.by laser, resectoscope)*** 3. ***Tubercular endometritis*** 4. ***Postradiation*** 5. ***Surgical remove of uterus*** | ***Uterine causes*** |
| 1. ***Premature ovarian failure*** 2. ***Resistant ovarian syndrome*** 3. ***Polycystic ovarian syndrome*** 4. ***pelvic radiation*** 5. ***ovarian tumer: eg.Granulosa cell tumor,Sertoli-leydig cell tumor)*** | ***Ovarian Causes*** |
| 1. ***Adenoma (eg.Prolactinoma)*** 2. ***Sheehan’s syndrome:*** *postpartum pituitary gland necrosis* 3. ***Cushing’s disease*** 4. ***Acromegaly*** | ***Pituitary Causes*** |
| 1. ***Psychological shock, stress, Anorexia nervosa*** 2. ***strenuous exercise*** 3. ***congenital malformation*** 4. ***Trauma : Accidents, surgery or radiotherapy*** 5. ***Infection : Tubercular or sarcoid granulomas*** 6. ***CNS Tumors : e.g. craniopharyngioma, meningioma*** | ***Hypothalamic factors*** |
| ***e.g.malnutrition, tuberculosis, chronic nephritis, diabetes,*** | ***Systemic causes*** |
| ***Hypothyroid state*** | ***Thyroid factors*** |
| 1. ***Adrenal tumor or hyperplasia*** 2. ***Cushing syndrome*** | ***Adrenal factors*** |
| 1. ***Contraceptive pills (post pill amenorrhea): absence of menstruation for 6 months following cessation of the combined oral contraceptive pill. Due to transient inhibition of gonadotrophin-releasing hormone.*** 2. ***Psychotrophic phenothiazine derivative drugs*** 3. ***Antihypertensive drugs like reserpine*** 4. ***dopamine antagonists*** | ***Iatrogenic***  ***druges*** |

***Management***

***History:***

1. *Mode of onset — whether sudden or gradual preceded by oligomenorrhea.*
2. *History of stress/psychological shock*
3. *History of eating disorder (anorexia nervosa).*
4. *Recent changes in weight (loss or gain)*
5. *History of physical exercise*
6. ***Appearance of abnormal symptoms*** *either coinciding or preceding the amenorrhea, such as:*

* ***Acne, hirsutism*** *(excessive growth of hair in normal and abnormal sites in female),* ***change in voice.***
* *(****galactorrhea)****:abnormal secretion of milk unrelated to pregnancy and lactation*
* ***Symptoms of hypothalamic-pituitary disease(*** *Headache, visual field defects, fatigue, polyuria, or polydipsia )*
* ***symptoms of estrogen deficiency****(Hot flushes, vaginal dryness, poor sleep, decreased libido )*

1. ***Obstetric history :***
   * *Cesarean section may be extended to hysterectomy of which the patient may be unaware.*
   * *Severe postpartum hemorrhage, or shock or infection.*
   * *Postpartum or postabortal uterine curettage. overzealous curettage leading to synechiae*
   * *Prolonged lactation — the patient may be amenorrheic since childbirth or she may have one or two periods, followed by amenorrhea. Even though the patient states that she is not breastfeeding her baby but she may putting the baby to the breast at night. This is sufficient to make the patient remain amenorrheic.*
2. ***Medical history :***

* *tuberculosis (pulmonary or extrapulmonary)*
* *diabetes*
* *chronic nephritis*
* *hypothyroid state*

1. ***Drug history:***

* *antipsychotics*
* *antihypertensive drugs like reserpine or methyldopa*
* *Recent use of oral contraceptive pill or its recent withdrawal*
* *radiotherapy and chemotherapy or surgery*
* *danazol*
* *high-dose progestogens*
* *metoclopramide*

1. ***Family history*** *— premature menopause often runs in the family (mother or sisters).*

***Examination***

***General examination***

* 1. *BMI—obesity as well as low BMI*
  2. *Evidence of thyroid disease, e.g. goiter, tachycardia, tremors*
  3. *Features of PCOS, e.g. hirsutism, acne, striae, acanthosis nigricans*
  4. *Signs of virilization, e.g. deep voice, clitoromegaly in addition to hirsutism, and acne*
  5. *Look for signs of Cushing syndrome(central obesity, moon face ,buffalo hump ,thin skin)*
  6. *Breast examination for galactorrhoea*
  7. *Fundoscopy, assessment of visual fields and CNS examinations if there is suspicion of pituitary tumor.*

***Abdominal examination***

* + 1. *Presence of striae associated with obesity may be related to Cushing disease.*
    2. *Mass in lower abdomen may be a malignant mass*

***Pelvic examination***

* 1. *Enlargement of clitoris.*
  2. *Genital examination for evidence of estrogen deficiency.*
  3. *Adnexal mass may be tubercular, tubo-ovarian mass or ovarian tumor.*

***Investigation:***

*The first step is pregnancy test; once the pregnancy has been ruled out do other investigation*

1. *a* ***CBC, urinalysis, and serum chemistries*** *should be carried out to rule out systemic disease*
2. *.for thyroid disease :****TSH,T3,T4***
3. ***Serum LH&FSH*** *:*

* *should be repeated after 6 weeks if >40 IU/L &30IU/L respectively*
* *This step helps to identify the site of deficiency of hormones (Pituitary or ovary)*
* *FSH >40 mIU/ml :indicates premature ovarian failure or resistant ovarian syndrome, this can be confirmed by ovarian biopsy*
* *Normal or low levels of FSH: indicates pituitary dysfunction.*

1. ***Serum Prolactin.*** *if galactorrhea*
2. ***Serum Testosterone***

* ***Androgen levels***
* ***total testosterone***
* ***SHBG***
* ***free androgen index (FAI):as the Androgen levels can be normal in PCOS***
* ***FAI = (total testosterone x 100) / SHBG***

1. ***The progesterone challenge test***

* *To evaluate ovarian production of estrogen indirectly.*
* *the administration of either:*

1. *medroxyprogesterone acetate (10 mg orally for 5–10 days)*
2. *or intramuscular progesterone (100–200 mg once)*

* *A positive test: withdrawal bleeding 2–7 days after completing the course indicates that HPO axis is normal, the ovaries are producing estrogen, functional uterus with an intact endometrium and a patent outflow tract.*
* *Modern measurement of serum estradiol levels is now usually sufficient to provide this evidence.*
* *If the patient does not bleed in response to progesterone this mean there is lack of progesterone receptor in endothelium*

1. ***Estrogen-progesterone challenge test:*** *course of OCP then observe if withdrawal bleeding occurs or not*

* *If there is no bleeding:local endometrial lesions like synechiae, which intern is confirmed by* ***HSG***
* *If bleeding occurs:endometrium is responsive but there is estrogen deficiency.*

1. ***GnRH stimulation test: If GnRH administered***

* ***increase pituitary gonadotropins( LH, FSH) indicate that the probable cause is hypothalamic dysfunction***
* ***no rise of gonadotropins( LH, FSH): indicate pituitary disorders***

1. ***Pelvic ultrasound*** *:*

* *evidence of polycystic ovary syndrome*
* *ovarian tumors*
* *Abnormalities of the lower genital tract.*

1. ***Pituitary MRI or CT scan for any pituitary tumors***
2. ***Hystrosalpigogram(HSG),Hysteroscopy to assess the uterus***
3. ***Karyotyping if required***

***Treatment***

***Is based on the etiology***

1. ***If no abnormality deleted:***

* *If patient is not anxious about amenorrhea :No treatment, but reassurance*
* *the patient is anxious about amenorrhea, start on OCP*

1. *If* ***Uterine causes***
2. ***Asherman s syndrom:****For synechiae:*

* *Adhesiolysis either by D& C or Hysteroscopic release of adhesions using scissors or electrocautery followed by insretion of IUCD*
* *To prevent recurrence of adhesion high dose estrogen and progestin therapy is given monthly for withdrawal bleed*

1. ***Cervical stenosis:*** *Careful cervical dilatation*
2. ***Ovarian Causes***
3. ***PCOS*** *:Depending on the woman’s desires*

* *Contraceptive pills to regularize the menses*
* *Ovulation induction to restore fertility*
* *Progestogen induced withdrawal bleeds to reduce the risk of endometrial hyperplasia.*

1. ***Premature ovarian failure****(spontaneous or iatrogenic)*

* *Hormone replacement therapy (HRT) to prevent bone loss (osteoporosis).*
* *Fertility is only a possibility by ovum donation and in vitro fertilization (IVF) and total replacement of hormones*
* *Corticosteroids in autoimmune disorders*

1. ***Ovarian tumor: excision***
2. ***Pituitary Causes***
3. ***Hyperprolactinemia***

* *Thyroxine if the hyperprolactinemia is due to hypothyroidism.*
* *Microadenomas—dopamine agonists such as bromocriptine and cabergoline*
* *Macroadenomas—may require surgery*

1. ***Sheehan's syndrome*** *:*

* *Treatment is lifelong hormone replacement therapy for the missing hormones*
* *Estrogen/progesterone therapy for restoration of menses.*
* *Gonadotropins for induction of ovulation*

1. ***Hypothalamic factors***
2. *Anxiety, stress: provide assurance and psychotherapy*
3. *Exercise induced amenorrhea :limit the physical activity*
4. ***Brain tumer eg.****Craniopharngioma,glioma treated surgically*
5. ***systemic causes***

*Malnourished and systemic illness: treat the cause*

1. ***thyroid factors***

***Hypothyroidism: thyroxine supplementation***

1. *Adrenal disorders: eg*

* *Adrenal tumor(simple adrenalectomy)*
* *For adult onset adrenal hyperplasia:dexamethasone*

1. ***Iatrogenic –druges:Contraceptive-related amenorrhoea:****The management is,*

*Expectant*

*Thank you*