Premature Ovarian Failure
Also called
Primary Ovarian Insufficiency

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Synonyms

- Primary ovarian insufficiency
- Premature ovarian failure
- Premature menopause
- Early menopause

Incidence

- 1 in 10,000 by age 20
- 1 in 1000 by age 30
- 1 in 100 by age 40
- 0.3% of women in reproductive age group
- 5-10% of women with secondary amenorrhoea

Diagnostic Criteria

- < 40 years of age
- 4 months of oligo / amenorrhoea
- S. FSH levels in menopausal range tested twice at least 1 month apart

Most women experience intermittent ovarian function rather than complete cessation of ovarian function. Hence complete amenorrhoea is not required for diagnosis

Ovarian failure ?

- 50% of spontaneously affected women have follicular activity
- 25% ovulate
- 5 – 10% conceive spontaneously

In women where ovarian failure is due to

- **Chemotherapy for malignancy**
- **↑ FSH and ↓ estrogen may be transitory and pregnancies have been reported in these women.**

Mechanism

Can be due to follicular dysfunction or follicular depletion can be due to several genes or structural abnormalities in X chromosome. In 90% cause is unknown.

The term premature ovarian failure should be replaced by ovarian

Insufficiency

or

Hypergonadotropic amenorrhoea

Hypergonadotropic hypogonadism

Clinical presentation

- Absent / Irregular menses / Infertility
- Hot flushes, night sweats
- Mood disturbances
- Changes in sleep cycle
- Dyspareuria due to estrogen deficiency

A few patients present with

- Primary amenorrhoea

  In these patients menopausal symptoms like hot flushes are rare.

Karyotyping Abnormalities

- Common in women with primary amenorrhoea
- Gonadal dysgenesis

Etiology

Family History

Family history of mental retardation

Ataxia

Abnormalities in FMRI gene

Premature ovarian failure

Polyglandular and Autoimmune disturbances

- 20% of women have autoimmune disease
- Hypothyroidism
- Adrenal insufficiency
- Hypoparathyroid
- Type I diabetes
- Dry eye syndrome
- Myesthe ?
- Rheumatoid arthritis
- SLE

Investigation

- Bone Mineral Density is usually less than in age – matched normal women
- Karyotypic abnormalities
- Single gene mutations
- Complex multifactorial polygenic inheritance

Diagnosis and Evaluation

Evaluation should be done in any woman with < 9 menses per year or missing more than 3 consecutive menstrual periods.

- Basal FSH
- TSH
- Prolactin

> 30 m iU / ml

Estrodiol (E2) < 50 pg/ml conc. and at least two occasions

If FSH is high, do

- Serum L.H
- TVS for ovarian follicle

Karyotype

To check for ‘Y’ chromosome and Turner syndrome

Absent or abnormal X chromosome

If turner is found – evaluation of aorta for any dilatation should be done

Testing for premutation of FMRI genes is warranted in young women with hypergonadotropic amenorrhoea

Also indicated:

- **Testing for adrenal Antibodies**
- **Serum TSH**
- **Thyroid stimulating immunoglobulins**
- **Thyroid peroxidase antibodies**
- **Ovarian antibodies → no test available**
- **BMD**

Management

- Diagnosis should be told gently
- Psychological support
- H.T. is indicated
- Data from WHI studies do not apply to young women

COC pills can be prescribed but they do not prevent pregnancy in these patients.

E2 - 17β 100 microgram transdermal

or

Oral conjugated estrogens (0.625mg – 1.25mg)

and

Micronized progesterone (100mg to 200mg)

or

Medroxy progesterone acetate 5 – 10mg for at least 14 days every 30 days

Androgen Deficiency

This also exists

Androgen replacement not validated

For increasing bone strength

1200 – 1500mg calcium

800 – 1000 in Vit D

} every day

Associated Conditions

- Adrenal insufficiency seen in almost 3% of women with POI
- Testing for presence of adrenal autoimmunity is recommended
- Patients who test +ve should have an annual corticotrophin stimulation test to assess adrenal function
- All patients should be told about symptoms of adrenal insufficiency and to report if such develop
- Hashimoto's Thyroiditis is also more common
- Dry eye syndrome is seen in 20% of these women

Infertility Management Options

a) Await spontaneous conception (pregnancy can occur in 5 – 10%)

b) Adoption

c) Oocyte donation

d) Embryo donation

Contraception

Low dose OCPs may not prevent pregnancy in these patients

To conclude

Primary Ovarian Insufficiency

a) Life changing diagnosis

b) Emotional and psychological support is the backbone of management

c) Physical health by taking care of

- Bone health
- Genetic health
- Hormone health
- Heart health

d) Infertility counselling for options

Primary Ovarian Insufficiency

H/o amenorrhoea / oligoamenorrhoea

Urine for pregnancy test – Negative

- S. FSH
- S. Prolactin
- S. TSH

- Age < 40 years
- S. FSH – 2 values in menopausal range more than 1 month apart

Tests indicated to find cause

a) Karyotype analysis that counts 30 cells so as to uncover mosaic chromosomal abnormalities

b) Testing for the FMR 1 Premutation

c) Measurement of adrenal antibodies by indirect immunofluorescence and 21-hydroxylase (CYP-21) immunoprecipitation tests

d) Pelvic ultrasound

e) Bone Mineral Density


THANK YOU