Premature menopause

Premature Menopause and Primary Ovarian Insufficiency:
The Gynecologist's Perspective

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Q1.What is the median age at Natural Menopause?
Ans:In Northern India the median age at menopause is 48 years,
In the U.S.it is 51 years (NAMS -2012)

Q2.What is the incidence of primary ovarian insufficiency(POI)?
Ans: The incidence of POI is very low i.e,1% in women below age of 40 and 0.1% in women under age of 30.

Q 3.What is the STRAW classification to stage Reproductive Aging?
Ans: Scientists from five countries and multiple disciplines evaluated data from cohort studies of midlife
women and recommended stages of menopausal transition1.

Q4.Which women can be defined to have gone into Premature Menopause or POI?
Ans: Women meeting thefollowing criteria can be diagnosed to have gone into POI:
Age < 40 years ,
with 4 months amenorrhea and
two serum FSH levels (usually over 40 IU/L) at least one month apart.

Q5.What are the important clinical features of Primary Ovarian Insufficiency?
Ans: Short Term: Vasomotor symptoms (hot flushes & night sweats)
Atrophic vaginitis
Dyspareunia
Primary or secondary amenorrhea
Infertility
Long Term : Bone & Cardiovascular Disease, Parkinson's Disease and decline in cognitive function
POI confers an advantage of Lower risk of breast cancer.
76% of POI develop after normal puberty and establishment of regular menses.
POI can occur after stopping hormonal contraceptive intake, failure to resume periods after pregnancy and prodromal menstrual disorders.
10% present with Primary Amenorrhea.
50% of POI patients have varying residual ovarian function and 5 to 10% achieve spontaneous conception.

Q6.What are the Etiologic mechanisms of Primary Ovarian Insufficiency.
Ans: The etiologic mechanism for primary ovarian insufficiency could be,
Genetic: Chromosomal abnormalities, Mutated POI related genes on X-chromosome,or Mutated POI-related genes on autosome .
Metabolic: classic galactosaemia, 17-OH deficiency.
Autoimmune; As an accompaniment of APS, dry eye syndrome, myasthenia gravis, rheumatoid

arthritis, SLE, etc.

Q7.What autoimmune disorders may associated by POI?
Ans: POI may be accompanied by Thyroid disorders(20%) autoimmune thyroiditis, Polyglandular failure Type I &IIHypoparathyroidism, Rheumatoid arthritis, ITP, Diabetes mellitus, Pernicious anaemia, Adrenal insufficiency(4%).

Q8.What are the modes of prescribing Hormone Therapy for Premature Menopause and POI?
Ans:HT for women with POI conveys minimal risk.NAMS recommends use of HT or oral contraceptives until the median age of natural menopause with periodic assessment. Well documented safety of supra-physiologic dosing of HT in women with POI. Formulations: COC pill, Combined HRT, Cyclic HRT, Transdermal patch100µgm/day, Estradiol gel, Progestogen containing IUD.**3**

Q9.Is there a role for Complimentary and Lifestyle Therapies in premature menopause?.
Ans: Regular weight bearing exercise is useful to prevent consequences of POI. It is important to avoid obesity. Emotional support of relatives and friends, limiting of alcohol, caffeine and cessation of smoking can also have positive influences in the management of premature menopause. , Calcium (1200 mg / day) + Vit D (800 IU / day) is useful to prevent osteoporosis in these women.

Q10.What are the tests for poor ovarian reserve?
Ans: Serum FSH, Oestradiol , AMH, No. of follicles (AFC)/ovarian volume, Inhibin B, Clomiphene Citrate Challenge Tests (CCCT), GnRHa Stimulation Test (GAST) are some of the tests to ascertain if a woman has a poor ovarian reserve.

Q11. What is the role of Anti- Mullerian hormone, an ovarian reserve marker in POI?
Ans: Anti-Mullerian hormone is a growth factor produced solely by small, growing follicles in the ovary. Serum levels strongly correlate with number of growing follicles. AMH levels are independent of the Hypothalamo Pitutary Ovarian (HPO) Axis. AMH levels decrease to undetectable levels at Menopause. In Cancer survivors, serum levels correlate with the extent of gonadal damage.

Q12. Fertility preservation is desirable in a small subset of patients with POI. Who are they?
Ans: If POI is diagnosed, while a patient has significant supply of oocytes, fertility preservation is desirable. It can also be considered in women about to undergo gonadotoxic chemotherapy, but who need future childbearing.

Q13. What are the Methods of Fertility Preservation?
Ans:Ovarian Transpositions, Embryo cryopreservation, Oocyte preservation, Ovarian tissue preservation, auto transplantion back to pelvis or subcutaneous tissue to be used for IVF when the woman is in remission of her cancer are some of the methods of fertility preservation in women who need it. .

Q14. Cancer survivors may go into premature menopause. What is the role of HRT in such patients?
Ans:Breast cancer : HRT NOT RECOMMENDED. Even vaginal estrogen is contraindicated
Endometrial cancer :HRT Contraindicated in low gradeEndometrial sarcoma; maybe used in patients with endometrial adenocarcinoma.
Ovarian cancer: HRT to be avoided in Granulosa cell tumors

Other cancers: Lymphoma, Leukemia's, Cervical cancer: to offer HRT upto median age(51yrs)3

Q15.Any method to prevent gonadotoxicity at the time of chemotherapy?
Ans:Yes, GnRHa – Goserelin 3.75, monthly along with each cycleof chemotherapy can prevent POI. Intramuscular or SubcutaneousGnRHagonists protects menstruation and prevents POI.3

Q16.Role of Prophylactic oophorectomy in Current Practice?
Ans:In the age group between 45 – 64 years usually 75% patients requiring Hysterectomy also undergo prophylactic oophorectomy.
Prophylactic oophorectomy is accompanied with a a high risk of Coronary Artery Disease(CAD),Stroke,Hip fractures, Parkinsonism,Dementia,
Cognitive impairment, depression and anxiety. 3
For 10,000 women, 47 fewer women will die of ovarian cancer but 838 more women will die from CHD and there will be158 more hip fractures if prophylactic oophorectomy is practiced. It can also have the following consequences:

8.6% excess mortality by 80 years
Even up to age 59 : 3.9% excess mortality
If a woman undergoing TAH with BSO were to have an average life span of 35 years after surgery, 1 out of 8 women undergoing prophylactic oophorectomies for benign disease will die prematurely3

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