CASE FOUR

Short case number: 3_29_4
Category: Endocrine and Reproductive Systems
Discipline: Obstetrics & Gynaecology
Setting: General Practice
Topic: Peri menopause and menopause

Case

49 year old Sally Schneider presents to your surgery complaining of "irregular" periods. Her periods can stop for 3 months then resume for a week or two and then stop again.

She has 3 children who are now all adults. She has no significant illness though there is Type II Diabetes in the family history as well as HT and IHD.

Questions

1. Define "the Menopause" and explain the physiological basis of the menopause using the "declining oocyte pool" model and by using this information is Sally "post menopausal"?
2. Again, using this model explain the physiology of Premature Ovarian failure and the most common causes.
3. Explain the major consequences of menopause by using the following time frames a) immediate and b) long term.
4. Using a graphical representation, show the difference in endometrial thickness (and pathology) between a normal cycle and an unopposed oestrogen effected cycle (include the long term possible changes)
5. Using your knowledge gained from the question above, what investigations could be relevant for Sally and WHY? What is the most significant pathological process that should concern you? State the site that this is likely to occur.

Suggested Reading

- Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier
- Dewhurst's Textbook of Obstetrics & Gynaecology, Edmonds K [editor]. Blackwell Publishing. 2007.

ANSWERS

<u>Question 1:</u> Define "the Menopause" and explain the physiological basis of the menopause using the "declining oocyte pool" model and by using this information is Sally "post menopausal"?

The menopause, from the Greek "menos" (month) and "Pausis' (cessation) is defined as the last menstrual period. The diagnosis can only be made retrospectively after a minimum of 1 year's amenorrhoea. Although the menopause occurs at an average age of 51, the physiological changes which result in the final menstrual period can start 10 years prior to this. This episode of dynamic neuroendocrine change is characterized by the 'climacteric', that is the climb to menopause.

<u>The declining oocyte pool.</u>

A newborn female infant has over a million oocytes. The oocyte cohort shrinks throughout life such that there are only a few thousand oocytes left as a woman enters her forties and few or none in the post menopause. It is the depletion of oocytes which eventually leads to the cessation of menstruation, the cardinal sign of the menopause.

Using this information Sally has not reached menopause, rather she is in the climacteric period, or 'peri menopause'.

<u>Question 2:</u> Again, using this model explain the physiology of Premature Ovarian failure and the most common causes.

Premature ovarian failure is said to have occurred when menstruation ceases before the age of 40 years. It occurs in 1% of women aged 40 years. Although there are many causes of early ovarian failure, the main cause is spontaneous or idiopathic.

Causes: Primary

- Chromosome abnormalities
- FSH receptor gene polymorphism and inhibin B mutation
- Enzyme deficiencies-hypothyroidism, Addison's disease, diabetes
- Autoimmune disease

Secondary

- Chemotherapy and radiotherapy
- Bilateral oophorectomy / surgical menopause
- Hysterectomy without oophorectomy
- Infection

Question 3: Explain the major consequences of menopause both immediate and long term

Consequences of the menopause:

Immediate:

Hot flushes and sweats are the commonest menopausal symptoms. Hot flushes are thought to arise due to loss of estrogenic induced opioid activity in the hypothalamus leading to thermodysregulation. Obese women are protected from these symptoms due to their production of large amounts of oestrone and their low sex hormone binding globulin levels.

Other symptoms include insomnia, anxiety, memory loss, tiredness and poor concentration. Mood disturbances can occur due to fluctuation in hormone levels leading to peri menopausal depression.

The menopause transition can also be associated with a significant reduction in sexuality and libido. This is not only because of decreased vaginal lubrication leading to dyspareunia but also due to the reduction in oestrogen levels. Psychological issues can also impact on libido: “no longer attractive”, “empty nest syndrome” etc.

Oestrogen deficiency leads to the rapid loss of collagen which contributes to the generalized atrophy that occurs after the menopause. In the genital tract this is manifested by dyspareunia and vaginal bleeding from fragile atrophic skin. In the lower urinary tract this can lead to dysuria, urgency and frequency.

Long term:

Osteoporosis, cardiovascular disease and dementia are three long term health problems which have been linked to the menopause.

Osteoporosis, or osteopenia, is a disorder of the bone matrix resulting in a reduction of bone strength to the extent that there is a significant increased risk of fracture. The hypo estrogenic state leads to activation of the bone remodelling units with an excess of bone resorption relative to formation. Women lose 50% of their skeleton by age 70 years, as compared to men who only lose 25%.

Cardiovascular: Women are protected against cardiovascular disease before the menopause, after which the incidence rapidly increases reaching a similar frequency to men by the age of 70 years. The protective effect of oestrogen in premenopausal women is thought to be mediated by an increase in HDL and a decrease in LDL, nitric oxide mediated vasodilation leading to increased myocardial blood flow.

CNS: Oestrogen also appears to have a direct effect on the vasculature of the CNS and promotes neuronal growth and neurotransmission. Studies have demonstrated that oestrogen may improve cerebral perfusion and cognition in women. In the long term this may prevent disease with a vascular aetiology such as vascular dementia and Alzheimer’s.

<u>Question 4:</u> Using a graphical representation, show the difference in endometrial thickness (and pathology) between a normal cycle and an unopposed oestrogen effected cycle (include the long term possible changes)

Oestrogen was originally used unopposed in non hysterectomized women. It was noted that this led to endometrial hyperplasia in up to 30% of cases. Progesterone has therefore been added to oestrogen therapy for the last 30 years to avoid hyperplasia and carcinoma.

Endometrial hyperplasia is classified into simple or complex depending on the glandular:stromal ratio; (much less stroma in complex hyperplasia) and "atypia" is added when there is increased nuclear:cytoplasmic ratio. 46% of women with atypical hyperplasia will have a concurrent adenocarcinoma and if not concurrent, there is a very high risk adenocarcinoma will develop. Therefore unless fertility desired hysterectomy recommended.

<u>Question 5</u>: Using your knowledge gained from the question above, what investigations could be relevant for Sally and why? What is the most significant pathological process that should concern you? State the site that this is likely to occur.

Sally's bleeding pattern has changed and it should be investigated. Phases of anovulation suggested by Sally's history (and therefore relatively unopposed oestrogen), diabetes and hypertension are all risk factors for endometrial carcinoma. If she was obese this would increase the risk still further. A protective factor is that she has had children.
Significant uterine pathology should therefore be excluded with a trans vaginal ultrasound, and an endometrial biopsy with outpatient endometrial sampling (eg Pipelle) or a D&C following referral to a gynaecologist. D&C often favoured.
If this is normal the explanation is "hormonal"/perimenopause.