CASE 2

Short case number: 3_18_02
Category: Endocrine and Reproductive Systems
Discipline: Obstetrics and Gynaecology
Setting: General Practice-Urban
Topic: Post-Menopausal bleeding

Case

Vera Carmody is 56 years old and has been post menopausal for 5 years. She presents following an episode of vaginal bleeding that lasted for 3 days. She is not taking any hormone replacement therapy and is otherwise well.

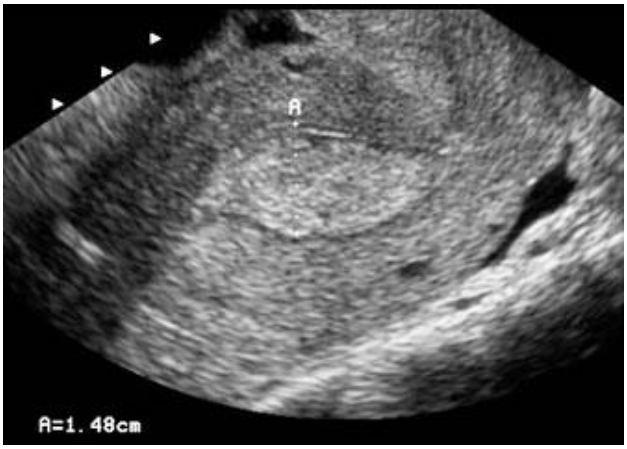
Questions

1. Define postmenopausal bleeding.

2. What are the key features of your history and why?

3. What are the key features of your examination and why?

4. You explain to Vera that you need to further investigate the bleeding to exclude malignancy. Describe the pathophysiology of endometrial hyperplasia, endometrial cancer and cervical cancer.



5. Vera's co-test for cervical screening is negative but the transvaginal ultrasound demonstrates thickening of the endometrium. What would you explain to Vera? What would be the next step in Vera's assessment and management?

6. You receive a letter back from the gynaecologist which informs you that Vera has been diagnosed with adenocarcinoma of the endometrium on endometrial biopsy. Briefly outline the process of staging that Vera will undergo.

Suggested reading:

1. Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier.
2. Kitchener HC. Cancer of the uterine corpus. in *Dewhurst's Textbook of Obstetrics & Gynaecology,* Edmonds K [editor]. Chap 57, pg. 645-650 Blackwell Publishing. 2007.

ANSWERS

1. Define post-menopausal bleeding.

Post-menopausal bleeding is vaginal bleeding greater than twelve months after menopause. [1]

2. What are the key features of your history and why?

- Any postmenopausal bleeding must be investigated to exclude endometrial cancer. Nature of the bleeding: persistent, recurrent, or heavy bleeding is more suggestive of an endometrial carcinoma. Post-coital bleeding might suggest a cervical lesion. Light pink staining may be from atrophic vaginitis. A watery discharge has been reported from carcinoma of the uterine tube.

- Risk factors for malignancy
    - Early menarche (<10 years)
    - Late menopause (>55 years)
    - Nulliparity
    - Unopposed oestrogen therapy
    - Obesity
    - Diabetes
    - Hypertension
    - Liver disease
    - Family History of Bowel Cancer/Uterine Cancer – HNPCC
    - DES exposure
    - PCOS
    - Proven or suspected germ-line mutation (Lynch syndrome/HNPCC)

- Other symptoms
    - Vaginal or vulval irritation
    - Bowel habit change
    - Abdominal discomfort, pain, swelling
    - Other vaginal discharge

- Local causes: use of a ring pessary, genital trauma, urethral caruncle or prolapse, urinary tract infection, abuse particularly in vulnerable populations.

- Drug use:
    - Hormones – prescription or "bio-identical", tamoxifen
    - Herbal / OTC preparations
    - Warfarin / Aspirin/ NSAIDS

- Cervical screening tests and mammography history

[1] Postmenopausal bleeding and discharge . In O'Connor V and Kovacs G. Obstetrics, Gynaecology and Women's Health. Cambridge press, Sydney, 2003. Pg 553

3. What are the key features of your examination and why?

General→ BMI, blood pressure
Pelvic –

- Inspection: vulval inspection (exclude vulval Ca), urethral meatus (exclude urethral caruncle – eversion). Cervix (exclude polyp, Ca) with cervical screening co-test and vagina (exclude Ca, Infections, atrophic changes).
- Bimanual palpation of pelvic organs checking for masses or tenderness.

4. You explain to Vera that you need to further investigate the bleeding to exclude malignancy. Describe the pathophysiology of endometrial hyperplasia, endometrial cancer and cervical cancer

Endometrial hyperplasia: Classified as either having:

- cellular atypia (endometrial intraepithelial neoplasia EIN), which has an 8 – 25% risk of progression to cancer, or co-existing cancer.
- not having cellular atypia (endometrial hyperplasia EH) which has a 1 – 3% risk of progression to cancer or co-existing cancer..

Endometrial cancer is the most common gynaecological cancer in Australia. The rate is rising with the increase in BMI. When diagnosed early the prognosis is good.

Type 1 endometrial cancer (endometrioid and mucinous adenocarcinomas) due to excess exposure to oestrogen, either increased circulating level or from normal levels unopposed by progesterone.

- obesity →peripheral conversion of androstenedione to oestriol
- diabetes→through actions of insulin-like growth factor 1,hyperinsulinaemia or increased oestrogen levels
- oestrogen producing tumour
- anovulatory cycles
- polycystic ovarian syndrome
- unopposed oestrogen used in HT (not conventional method of HT: i.e. always prescribe oestrogen and progesterone if uterus present. Unopposed OK if had hysterectomy).

Type 2 endometrial cancer (serous papillary and clear cell) →not oestrogen driven → Mutation of p53, a tumour suppressor gene is associated with 20% of endometrial cancer → 50% mortality.

Cervical cancer

Squamous cell carcinoma of the cervix → involves invasion of cells into the underlying stroma with desmoplastic response (stromal reaction).

Glandular lesions of the cervix → adenocarcinoma in situ is defined as replacement of endocervical glandular epithelium by cytologically malignant cells without evidence of stromal invasion → associated with HSIL (high grade squamous intraepithelial lesion – on cytology in 50 per cent of cases.

Other → numerous others can develop including sarcomas/melanoma, lymphoma/metastatic →from endometrium, vagina, ovary, bladder, bowel, colon, stomach and breast

5. Vera's cervical screening co-test is negative but the transvaginal ultrasound demonstrates thickening of the endometrium with no ovarian cysts. What would you explain to Vera? What would be the next step in Vera's assessment and management?

15% of women with post-menopausal bleeding will have endometrial cancer → investigation entails referral to a gynaecologist for hysteroscopy and endometrial biopsy. Pipelle sampling is only useful when the histology shows endometrial cancer (10% false negative rate).

6. You receive a letter back from the gynaecologist which informs you that Vera has been diagnosed with adenocarcinoma of the endometrium on histology of uterine curettings. Briefly outline the process of staging that Vera will undergo.

The pattern of spread in endometrial cancer is generally through the myometrial thickness to the serosal surface of the uterus and then involvement of the ovaries and fallopian tubes. At any point lymph node metastases may occur but the majority of lymph node metastases are found in association with deeper involvement of the myometrium.

Staging is surgical with evaluation of the pelvic (stage III) and para-aortic nodes (stage IV) → no specific investigations other than a CXR although many gynaecological oncologists request a pre-operative CT scan of the chest, abdomen and pelvis → tumour volume is the most important prognostic factor. More recently MRI scans have been used to stage radiologically.

- Stage I: tumour is confined to the corpus uteri.
- Stage II: tumour involves the corpus and the cervix, but has not extended outside the uterus.
- Stage III: tumour extends outside of the uterus but is confined to the true pelvis
- Stage IV: tumour invades bladder or bowel mucosa or metastatic spread to distant sites.