Mini Review
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Clinical perspective to postmenopausal bleeding and its diagnostic evaluation: a mini review

Abstract

Postmenopausal bleeding is a sinister in it and refers to any uterine bleeding in a menopausal woman and warrants an urgent evaluation to rule out carcinoma of either uterine or extrauterine origin. Meticulous history taking and physical examination is must to formulate the probable differential diagnosis. Endometrial evaluation should then be followed by the most appropriate test available. The main aim of this review is to highlight the gravity of postmenopausal bleeding and to make the best choice among the disparate tests available to ensure timely diagnosis.

Keywords: postmenopausal, endometrial, thickness, transvaginal, ultrasonography, endometrial, cancer, bleeding, gynaecological, atypia

Volume 8 Issue 1 - 2019

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Received: Januvary 04, 2019 | **Published:** January 24, 2019

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Approach to a patient with postmenopausal bleeding

Postmenopausal bleeding refers to any uterine bleeding in a menopausal woman, accounting to nearly 5 % of all outpatient visits to a gynaecologist.[1] Among the 454 postmenopausal patients in one of the study, final diagnosis was cancer in 6.6% cases, atypical hyperplasia in 0.2%, hyperplasia without atypia in 2%, polyps in 37.7%, fibroid in 6.2%, proliferative/secretory in 14.5% and hypertrophy/atrophy in 30.8% cases.[2] The causes of postmenopausal bleeding can be gynaecological or non- gynaecological. Among the gynaecological causes it can be either intrauterine or extrauterine and these includes cervical, vaginal, vulval, or from fallopian tube and ovaries. Bleeding from urethra, bladder, anus, rectum, bowel or perineum should also be ruled out.

Differential diagnosis of postmenopausal bleeding is discussed in brief here:

Atrophy

Hypoestrogenism leads to endometrial atrophy which due to friction can lead to micro erosions and thus bleeding.

Carcinoma

In one of the largest metanalysis based on ninety-two studies, a 9 % risk of endometrial carcinoma was found in patients with postmenopausal bleeding. Subset analysis of the same study, found the incidence of carcinoma in patients with postmenopausal bleeding and endometrial thickness of 4-5 mm as 19%.[3] Uterine sarcoma constitutes only 3-5% of all uterine tumors and these cancers originate from the stroma of the endometrium or myometrium. Fallopian tubes, ovarian, cervical, vaginal carcinomas can also present as vaginal bleeding.

Vulval cancer in advanced stage can present as postmenopausal bleeding. Choriocarcinoma is also a rare cause in minority.[4]

Polyps/endometrial hyperplasia

These are benign growth and are estrogen dependent.

Fibroids/adenomyosis

Rare causes in this age group.

Hormone therapy/anticoagulants/hormonal medicine containing soy

Post-radiation therapy

Endometritis

Uncommon cause, but tubercular endometritis is seen in developing nations.

Trauma, foreign body like pessary

Diseases of adjacent organs like diverticulitis, urethritis, bladder infection or cancer, haemorrhoids.

Meticulous history taking, physical examination and endometrial evaluation are the key to diagnose the cause of bleeding to ensure optimal management. History should include duration of menopause, duration of bleeding, its nature, associated symptoms like pain abdomen, fever or bladder or bowel symptoms, precipitating factor if any, medications being taken and family history of breast, colon and endometrial cancer. Pain is extraordinary and is characterised by Simpson's pain and is noted in 15% cases. The pain is referred to hypogastrium or to both iliac fossa and tends to appear at the same time each day lasting 1-2 hours. General examination includes BMI (body mass index), blood pressure, lymphadenopathy (supraclavicular, axillary, inguinal), abdominal examination to look for ascites, hepatomegaly, omental metastasis. Local examination is also done including per-speculum examination to look for local causes, bimanual examination for uterine size and adnexal masses and also per-rectal examination for parametrium and involvement of rectal mucosa. The main objective of evaluation of the patients presenting with postmenopausal bleeding is to rule out endometrial carcinoma, when other extrauterine and non-gynaecological causes have been ruled out. The methods of endometrial evaluation can be invasive or non-invasive.

Dilatation and curettage

This is one of the oldest techniques and not used now days, except in few cases when office endometrial biopsy is not possible or tissue retrieval is inadequate and there exist high possibility of endometrial cancer.

Endometrial biopsy

Histopathological diagnosis is must in cases of postmenopausal bleeding who are at high risk for endometrial cancer. Even in patients with persistent or recurrent bleeding and TVS suggestive of endometrial thickness less than 3 mm, endometrial biopsy is required. Advantages of biopsy include no cervical dilation/ no anaesthesia

required and pipelle device is among the best device available. Sensitivity for diagnosing endometrial cancer in postmenopausal patients was 99.6% and for atypical hyperplasia, it was 81% and specificity was 98-100% according to one of the meta-analysis of 39 studies involving 7914 women.[5] Endometrial sampling was found to be more reliable when at least half of the endometrium was affected with the disease. If endometrial biopsy yields insufficient tissue for pathological diagnosis, then clinical scenario guides further management and in majority cases transvaginal ultrasonography is done.

Hysteroscopy

It provides direct visualization of endometrial cavity, thereby allowing targeted biopsy of the lesion identified during the procedure. This procedure requires more skill and is costly.[6] there exist a small risk of intra-peritoneal spread of endometrial cancer cells, but further studies are required to confirm the same.

Transvaginal ultrasonography

Sagital view of the uterus is the best view to measure endometrial thickness in antero-posterior dimension from one basalis layer to the other excluding any fluid in the cavity. In patients with axial uterus, obesity, coexisting myomas, adenomyosis or previous uterine surgery, it is sometimes difficult to measure endometrial thickness accurately. Endometrial thickness (ET) of less than 4 mm as per American College of Obstetrician and Gynaecologists (ACOG) and 5 mm as according to Society of Radiologists in Ultrasound (SRU) is associated with low risk of endometrial cancer.[7,8] ACOG advices TVUS as second line test when endometrial sampling yields insufficient tissue. The sensitivity and specificity of TVUS at 4mm endometrial thickness was 96% and 53% and at 5mm it was 96% and 61% respectively in identifying all possible cases of carcinoma.[9] Asymptomatic women with increased endometrial thickness and endometrial fluid coexist in 5-20% of patients and thus needs an evaluation. In all these cases, clinical acumen is the most important guide. In one of the studies, it was suggested to evaluate any patient with endometrial thickness of more than 11 mm and for women with endometrial fluid and ET more than 3 mm and in all these cases, biopsy is required.[10]

No cut off for ET has been suggested in any study for patients on hormone therapy or tamoxifen.

1. Saline infusion sono-hysterography
2. The most important benefit of this modality is evaluation of uterine cavity to detect polyps or submucous fibroids. Sensitivity and specificity of polyps are found to be 93% and 94% respectively.[11] Even in this, the small risk of intraperitoneal spread of endometrial cancer cells exists.
3. MRI and CECT scan are further test available which can further help in making the diagnosis and substantiate management.

Conclusion

So, to conclude postmenopausal bleeding is a sinister in itself and its appropriate and timely intervention is must. Endometrial atrophy and polyps are the most common causes and around 9 % of all these cases presents with endometrial carcinoma. The primary aim of the evaluation in these cases is to exclude malignancy and either endometrial biopsy or TVUS can be the initial test depending on the clinical scenario. A review of literature revealed that endometrial thickness as measured by TVUS of less than 4mm have false negative rate of detection of endometrial cancer of 0.25%-0.5%, which is comparable to that reported with endometrial biopsy. Persistent or recurrent bleeding needs further evaluation even in cases with ET less than 4 mm, especially in association with other risk factors. Endometrial biopsy can be used as the primary test or following ultrasonography. If blind endometrial sampling does not reveal any significant pathology and patient is high risk, further evaluation with hysteroscopic guided biopsy should be done. Evaluation for extrauterine causes of bleeding, such as cervical, fallopian tube or ovarian cancer should also be done. Management as per the identified cause should then be planned. Further studies on larger population are required to define the cut–off for endometrial thickness for patients on hormonal therapy and on tamoxifen, so that they can be evaluated timely. Also, the small risk of spread of malignant cells intraperitoneally with hysteroscopy and SIS, also need to be evaluated.

Acknowledgments

None.

Conflicts of interest

The author declared that there are no conflicts of interest.

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