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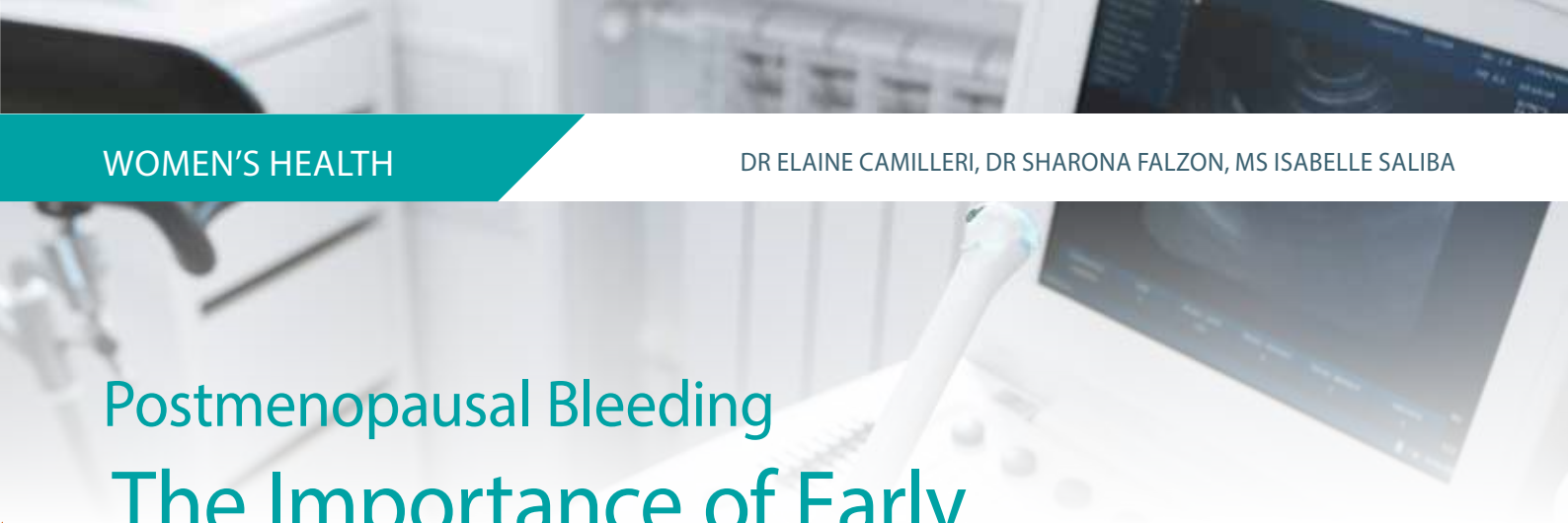

Postmenopausal Bleeding

The Importance of Early Diagnosis in Improving Prognosis

ABSTRACT

Postmeopausal bleeding (PMB) is defined as vaginal bleeding that occurs at least twelve months after a woman's last period. It is a common complaint with a broad differential diagnosis but endometrial cancer must be excluded. About 10% of women over 55 years who present with PMB are at risk of gynaecological cancer and should be investigated promptly. This article highlights the importance of timely diagnosis by healthcare professionals to improve the prognosis of patients with malignant aetiologies. Mater Dei Hospital has a specific fast track clinic for patients with PMB which ensures that patients are seen in a timely manner.

KEYWORDS

Postmenopausal bleeding (PMB), endometrial cancer, endometrial hyperplasia, transvaginal ultrasound.

INTRODUCTION

Menopause is the time in a woman's life when fertility naturally wanes. The average age is around 51 years when the oestrogen levels decline leading to cessation of menstrual periods. It is a retrospective diagnosis, as it can only be confirmed after 12 months of amenorrhoea from the last menstrual period. PMB is defined as bleeding after this time period and it should be investigated. It is a common complaint and its differential diagnosis includes physiological changes of the reproductive tract, benign conditions, as well as malignant conditions. Endometrial cancer is the most common gynaecological malignancy.

This often presents at an early stage when it is possibly curative. Hence, early diagnosis is crucial for a good prognosis.

AETIOLOGY

PMB can be caused by both benign or malignant, gynaecological or non-gnyaecological aetiologies, The most common cause of PMB or spotting is endometrial or vaginal atrophy (also referred to as non-infective endometritis or vaginitis). This is part of the physiological changes that happen in the reproductive tract as the oestrogen levels decline during menopause.

Causes of PMB include the following:

- Polyps which can occur in the endometrium or cervix. They bleed secondary to venous stasis and apical necrosis caused by stromal congestion.
- Endometrial hyperplasia.
- Malignancy: Bleeding secondary to vascular fragility or invasion of the cancer into nearby vessels. In this case PMB is usually attributed to an intrauterine malignancy but any cancer along the genital tract can give rise to PMB: cervical, endometrial, fallopian tube, ovarian, vaginal and vulvar carcinomas.
- Infection along the genital tract cause inflammation and irritation that leads to bleeding.
- Medications such as tamoxifen, and hormone replacement therapy (HRT), as well as herbal supplements (phytoestrogens) may stimulate proliferation of the endometrial lining and subsequently result in bleeding. Antithrombotic therapy may increase the bleeding risk as well.
- Insertion of foreign bodies such as pessaries may cause abrasions resulting in bleeding.

The etiology of bleeding may also be non-gynaecologic i.e. disease in adjacent structures may be mistaken for vaginal bleeding. Bleeding from the urethra (caruncle, diverticulum, urethritis), from bladder (cystitis, malignancy or renal disease leading to hematuria) as well as from bowel (fissures, polyps, colitis, haemorrhoids and malignancy).[1]

EPIDEMIOLOGY

About 4-11% of postmenopausal women report vaginal bleeding.[1] Of these, around 5% present to their gynaecologist and only 10% of those that present to their gynaecologist have endometrial cancer.[1]

91% of cases of endometrial cancer occur in postmenopausal women. Most cases of endometrial carcinoma are adenocarcinomas in origin and are

associated with exposure of oestrogen unopposed by progesterone. It is the most common gynaecological malignancy in women. Risk factors include nulliparity, anovulatory cycles such as polycystic ovarian syndrome, obesity, type 2 diabetes mellitus and hypertension, genetic syndromes such as Lynch syndrome and exogenous unopposed oestrogens.

DIAGNOSIS

A comprehensive history is key to understanding PMB, and menopausal status should be established first. Risk factors for adenocarcinoma should be explored in the medical history. Clinical examination allows a thorough evaluation of the internal and external anatomy of the genital tract. A bleeding site may be identified such as lacerations or lesions on the anus, urethra, external genitalia or cervix. A smear test is recommended even if older than 65 years of age.

In addition to clinical evaluation, a transvaginal ultrasound (TVUS) is the initial investigation of choice.[2] Endometrial thickness (ET) measures the anterior-posterior length of maximal endometrial echo thickness in the long axis view of the uterus. TVUS can also identify adnexal pathology and leiomyomas. An ET equal to or less than 4 mm on scan has a negative predictive value approximately 96-99%. Hence, endometrial sampling is not required below this cut-off value, unless symptoms are recurrent.[3]

Endometrial sampling is necessary if the TVUS shows (in symptomatic women):

1. An ET >4 mm.
2. Increased echogenicity or heterogeneity on scan (both diffuse or locally).
3. Endometrium is not visualised properly.
4. Patients with persistent PMB even if ET <4 mm.

The American College of Obstetricians and Gynaecologists also suggests that in patients with a higher pretest probability for malignancy, endometrial sampling can be used first rather than ultrasound. This is because the 4 mm ET threshold may miss endometrial cancer in 1 in 339 patients.[2,3]

ACCURACY OF ENDOMETRIAL SAMPLING

The accuracy of endometrial sampling correlates with the amount of tissue obtained. Several methods have been used but dilation and curettage is the one which has been most widely used. It is around 90% sensitive.[4] However, less invasive outpatients methods include hysteroscopic biopsies using the Pipelle device or Vabra aspirator. These are very sensitive, with detection rates of 99.6% and 97.1%, respectively.[4,5]

Women with an insufficient sample on biopsy can be reassured and discharged only if there is hysteroscopic evidence of endometrial atrophy and a negative scan (ET less than or equal to 4 mm). Re-investigation is necessary if symptoms recur (for example there may be failure of detection of a small polyp in an atrophic endometrium due to the low cell yield in the sample) (Figure 1).

On the other hand all women with an insufficient sample which have hysteroscopic or ultrasonographic evidence of endometrial thickening or had a recurrent PMB should have an inpatient hysteroscopy and endometrial sampling (Figure 1).[3]

Hysteroscopy allows direct macroscopic visualisation of abnormal endometrium and samples are obtained directly from the lesion.

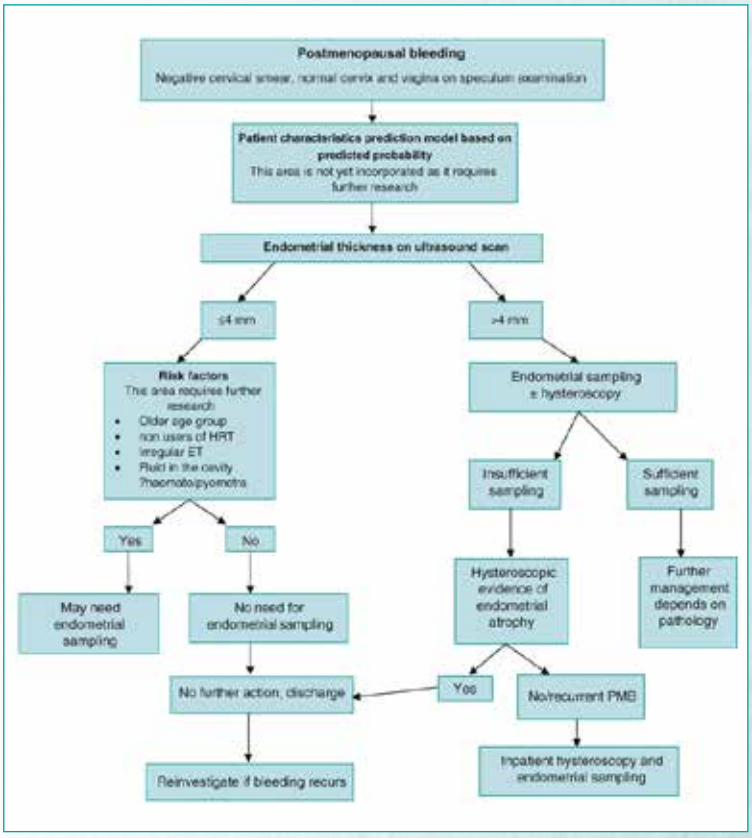

Figure 1: Scheme summarizing the immediate and long-term effect of estrogen decline during menopause.[2]

Decisions about further investigations should be taken on a case by case basis and risk factors for endometrial cancer should be considered. Indeed, current literature states that asymptomatic ET between 8 to 11 mm in postmenopausal women is not abnormal in the first year after the last menstrual period since the endometrium may be thicker secondary to some residual hormonal activity.[6]

Other positive findings on TVUS in asymptomatic women (i.e do not present with PMB) that should be referred for further investigations include inhomogeneous endometrium, ET >11 mm, particulate fluid and increased vascularity.[1]

An effective method for investigating asymptomatic postmenopausal women with an ET of >6 mm is hysteroscopy as the commonest pathology in these cases is endometrial polyps.[5]

MANAGEMENT

The aetiology of PMB dictates the management.

Vaginal atrophy is usually self-limiting but may be treated with vaginal oestrogen or lubricants.

Polyps should be removed hysteroscopically. Polyps are often benign but in 5% cases hyperplasia or malignancy may be found.

Endometrial hyperplasia is classified as hyperplasia with or without atypia. In hyperplasia without atypia the risk of progressing to malignancy is less than 5% over 20 years and most cases regress spontaneously. Observation alone with regular biopsies for follow-up is advised, especially if reversible factors are identified, such as obesity and HRT. However, progesterone treatment (oral or intrauterine for at least 6 months) is indicated in women who, despite observation and follow-ups, failed to regress or are symptomatic with abnormal bleeding. On the other hand, in hyperplasia with atypia, hysterectomy with bilateral salpingo-oophorectomy is the best treatment option. If women are not fit for surgery or they want to preserve fertility, a pretreatment evaluation should be performed to rule out invasive cancer or pre-existing ovarian pathology. First line is intrauterine levonorgestrel, and oral progestogens are the second best option. Once fertility preservation is not an issue then hysterectomy should be offered.[7]

In endometrial carcinoma hysterectomy with bilateral salpingo-oophorectomy followed by staging is recommended. In some circumstances, omentectomy is required. Conservative medical management is the same as above. In advanced cases, palliation of symptoms using high-dose progesterone and external beam radiotherapy to control bleeding should be used.

Fast track PMB clinic in Mater Dei Hospital

Mater Dei Hospital Gynaecology outpatients offers a Fast-track clinic service. The aim of this PMB clinic is to provide the highest quality, evidence-based service for all women presenting with PMB. Referrals to this clinic have to be vetted within 2 weeks. The healthcare professionals in this clinic will perform history taking, preliminary diagnostic investigations (including a TVUS and if the ET is more than 4 mm, endometrial biopsies are performed using a pipelle), counselling and continuing management. An outpatient follow-up appointment is then arranged for the histology result. Our patients benefit from early diagnosis and reduced number of appointments and clinic visits.

Competing interests and funding statements

There are no competing interests to declare. No funding has been received.

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