Histopathological spectrum of lesions in women with postmenopausal bleeding

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Abstract

Introduction: Postmenopausal bleeding is regarded as an omnious and serious alarm of genital pathology. It is a symptom having various etiology and has a strong association with malignancy, which demands its thorough evaluation.

Aims and Objectives: The present study was carried out to know the causes of postmenopausal bleeding based on histopathology and the percentage of various benign premalignant & malignant lesions in postmenopausal bleeding. The association with age was also studied.

Methodology: This study included 139 specimens received in in Department of Pathology MMC & RI Mysore, with history of postmenopausal bleeding, from January 2013 to December 2014.

Results: Mean age of the patients in the study was 57 years. Cervical biopsy was most common biopsy received (43.8%). Benign cases were 51.6%, malignant cases 36.07% and premalignant lesions were 9.27%. Among the benign lesions atrophic endometrium was most common (11.2%). Cervical cancer was most common (33%) among malignancy.

Conclusion: Any patient presenting with history of postmenopausal bleeding should be investigated thoroughly to determine the cause of bleeding. Cervical lesions are still the most common cause postmenopausal bleeding so screening programme should be effectively implemented.

Keywords: Postmenopausal bleeding, Histopathology.

Introduction

Menopause is taken from the Greek word "Meno" (month) & "pause" means stop. Menopause occurs physiologically in women who are about the age of 50.[1] Most women all over the world attain menopause at 45-55yrs with the average age 51 yrs.[2] Vaginal bleeding which occurs after one year of amenorrhea in a woman of the age in which menopause can be expected is defined as postmenopausal bleeding.[3] In gynecological practice PMB represents for 5% of cases.[4] Cancer is an important cause of this abnormal bleeding, with the dictum is that postmenopausal bleeding indicates malignancy until proven otherwise.[5-17] The dictum is that postmenopausal bleeding always indicates malignancy until proven otherwise.[11] In postmenopausal women with vaginal bleeding the probability of endometrial carcinoma is approximately 10%.[18] Malignant tumors account for 7-49% of cases of PMB and this depends on racial, genetic, ethnic differences in incidence of malignancy in diverse population as well as to different criteria adopted by different studies. The present era life expectancy of women have increased & most will experience the postmenopausal phase. The chances of malignancy increases with increase in age of onset of PMB. Most studies on PMB are based on endometrial biopsies. Since few of studies describing the histological spectrum of lesions in entire genital tract the present study was undertaken to examine the lesions in genital tract in cases of PMB.

Aims and Objectives

The present study was carried out to know the causes of postmenopausal bleeding based on histopathology and the percentage of various benign premalignant &malignant lesions in postmenopausal bleeding. The association with age was also studied.

Materials and Methods

The present study was conducted for a period of 2 years from January 2013 to December 2014 at Department of Pathology, MMC&RI. Material for study was collected from endometrial, cervical, vaginal, vulval biopsies and hysterectomy specimens which were sent for histopathological examination to Department of Pathology from clinically diagnosed cases of postmenopausal bleeding. The History noted were spotting per vagina, brownish discharge, scanty flow and moderate to profuse bleeding. Premature menopause whether surgical or natural, with age <40yrs and patient on hormonal replacement therapy/on anticoagulant/having bleeding disorders were excluded from the study. After the collection of detailed data, the specimens were examined grossly. Specimens were fixed in 10% buffered formalin. Sections were processed and stained with H & E. Slides were examined under microscope and observations were done. The results were compiled, analysed using proportion and compared with other studies.

Results

The study comprised of 139 cases which met the inclusion criteria were taken for this study. Age of the patients with post menopausal bleed (Table 1) ranged between 41-80 years with the mean age of 57yrs. The maximum number of cases 36(25.8%) were between the age group of 46-50 years. The most common site biopsy received were from cervix, 61(43.8%). (Table 2)

Postmenopausal bleeding was due to benign causes in 78 cases (51.6%). (Table 3) Atrophic endometrium was the commonest benign cause comprising total 19 cases (11.7%). Proliferative endometrium 15 cases (9.2%), endometrial hyperplasia without atypia 11 cases (6.7%), cervicitis 6 cases (3.7%), cervical polyp 6 cases (3.7%), endometrial polyp 5 cases (3%), adenomyosis 3 cases (1.55%), leiomyoma 3 cases(1.55%) and one case of endometritis (0.6%) & one case of prolapse(0.6%). Inadequate samples were 11 cases (6.7%).

Most of the malignant tumors were from the cervix 55 cases (33%) (Table 3) followed by uterine malignancy 15 cases (9.2%), Carcinoma vulva 3 cases (1.85%), Carcinoma vagina 2 cases (1.23%). The ratio of malignant tumor in cervix to those in uterus was 2.9:1 (Table 4). Among the malignant lesions squamous cell carcinoma was the most common 46 (28.35%). The number of benign lesions added up to more than 100% as these lesions overlapped that is one specimen had more than one lesion.

Table 1: Distribution of study subjects according to age groups

AGE (years)	No of study subjects	Percentage
41-45	11	7.9
46-50	36	25.8
51-55	28	20.1
56-60	26	18.7
61-65	18	12.9
66-70	13	9.3
>70	6	4.3
>80	1	0.7
Total	139	100

Table 2: Type of specimens received

Type of specimen	Numbers	Percentage
Biopsy vulva and vagina	4	2.83
Biopsy cervix	61	43.8
Biopsy cervix and endometrium	13	9.3
Endometrial curettage	42	30.2
Hysterectomy	7	5.03
Hysterectomy with adnexa	11	7.9
Hysterectomy with adnexa, omentum and lymph nodes	1	o.7
Total	139	100

Table 3: Distribution and percentage of various lesions

S. No	Histopathology diagnosis	Number	Percentage
1	Indequate	11	6.7
2	Cervicitis	6	3.7
3	Cervical polyp	6	3.7
4	Atrophic endometrium	19	11.7
5	proliferative endometrium	15	9.2
6	Endometrial hyperplasia without atypia	11	6.7
7	Endometrial hyperplasia with atypia	3	1.85
8	Endometrial polyp	5	3
9	Endometritis	1	0.6
10	Adenomyosis	3	1.85
11	Leiomyoma	5	3
12	Prolapse	1	0.6
13	Carcinoma cervix(total)	55	3
	CIN	11	6.7
	SCC	42	25.9
	Undifferentiated	2	1.23
14	Malignant Uterus (Total)	15	9.5
	Adenocarcinoma	1O	6.2
	Adenosquamous carcinoma	2	1.2

	Papillary Serous Carcinoma	2	1.2
	MMMT	1	0.6
15	Carcinoma Vulva (SCC)	3	1.85
16	Carcinoma Vagina (SCC and Adenocarcinoma)	2	1.23
	Total	162	100

Table 4: Distribution of lesions

S. No	Histopathology	Number of cases	Percentage
1	Benign	78	51.6
2	Malignant	59	39.07
3	Premalignant	14	9.27
	Total	151	100

Discussion

PMB means bleeding from genital tract occurring in postmenopausal women after 12 months of amenorrhea in a women of postmenopausal age.[19] PMB is frequent and accounts for 5% of gynecological presentations.[4] In PMB the incidence of malignancy is very high, so it requires immediate investigations for early diagnosis, follow up and prompt treatment. In present era life expectancy has increased and women tend to live longer and many will experience the postmenopausal phase. PMB is a very alarming sign that may be associated with cervical or uterine malignancy.

The investigations and assessment is moving away from operation theatre, ward environment into outpatient department. However the primary assessment in all cases of PMB should be trans vaginal ultrasound scanning(TVS) as the thickening of endometrium may indicate significant pathology.[20]The present trend in investigating only lesions with PMB when endometrial thickness is >4mm as measured by ultrasound.[21] However the authors have recommended systematic collection of biopsies from symptomatic patients[22] because there have been reports of cancer in patients presenting with ultrasound measured endometrial thickness <5mm.[23]

In the present study it was noted that maximum number of cases that is (25.8%) were in the age group of 46-50 years while minimum number of cases(7.9%) were in 41-45 yrs. In the present study age range was from 41-80 yrs while the study done by Way sf et al, Sousa R et al, Bharani B et al and Sheikh M et al was 38-94, 43-82,52-65, 42-84 yrs respectively.[24-27]

Mean age of the present study was 57yrs whereas in other studies it was 47.43 to 56.5yrs.[28] It was also noted that as the age of subjects increases the incidence of PMB decreases which shows an inverse relationship between age and age of PMB. In study done by Gredmark T et al, the number of cases of PMB decreased with increasing age.[16]

In this present study 139 samples were received which were biopsy specimens from cervix, endometrium, vulva, vagina and hysterectomy specimens. Benign conditions were 51.6%, malignant 39.07% and premalignant 9.27%. (Table 5) Benign conditions included cervicitis, cervical polyp, atrophic endometrium, proliferative endometrium without atypia, endometrial polyp, endometritis, adenomyosis, leiomyoma and prolapse. It was noted that atrophic endometrium (Fig. 1) was the most common histological lesion in benign conditions that is 19 cases (11.7%), followed by proliferative endometrium 15 cases (9.2%). (Table 6) But atrophy was found to be 49.9% by Gredmark et al,[16] 52% by Lee WH et al,[12] 16.3% by Naik et al,[11] 32% by Cheema et al.[2] The probable explanation for unexplained bleeding from atrophic endometrium are fluctuation of serum levels of estrogen, nonspecific chronic endometritis, sclerotic degeneration of myometrial arterioles, associated diabetes mellitus & hypertension, uterus prolapse causing passive congestion& bleeding, rupture of endometrial cysts.[29]

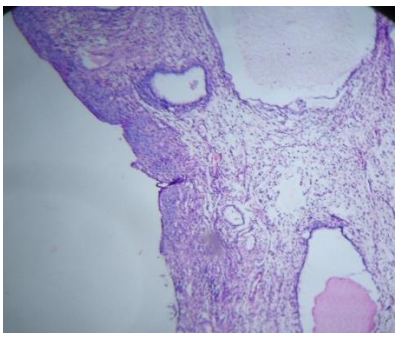

Fig. 1: Atropic endometrium(H&E x 10x)

In the present study it was noted that proliferative endometrium was in 15 cases (9.2%) which is comparable to study of Naik et al[11] who found it to be 8.6% and Cheema et al 8%.[2] Choo YC et al found out that stimulation of postmenopausal endometrium can occur because of conversion of adrenal androsteinedione by peripheral fat to estrogen which leads to proliferative endometrium and also fluctuation of low level of estrogen results in bleeding from proliferative endometrium.[30]

Table 5: Ratio of cervical and uterine cancer in different studies

Study	Ratio of cervical and uterine carcinoma
Lee et al	1.2:1
Tyagi et al	2.6:1
Present study 2015	2.9:1

Table 6: Distribution of various lesions in different studies

	Lee 1995	Gredmark 1995	Naik 2005	Cheema 2008	Tyagi 2010	Present Study
Ca vagina and vulva	0.6				4.3	1.23
Ca cervix	12.9		39	14	34.5	33
Ca uterine	11	8	9.6	10	13	9.2
Ca ovary	1.2		0.96	6	5.5	
Cervicitis	12.9		2.8	68	2.1	3.7
Polyp	6.7	9		16	16	3
Proliferative endometrium		4	8.6	8	1.5	9.2
Secretary endometrium		1		14	1.2	
Atrophic endometrium		50	16.3	32	2.4	11.7
Endometrial hyperplasia	3.1	10	13.4	2	4.9	8.5
Leiomyoma	4.3				1.8	1.85
Endometritis	1.2					0.6
Inadequate	24.5	14		4	5.2	6.7

In endometrial polyp bleeding can be as a result of injury to thin walled vein below surface epithelium or thrombosis of the vessels. The bleeding in leiomyoma can occur due to congestion or atrophy& thinning of overlying endometrium and myometrium results in ulceration and bleeding.[31]

PMB due to malignant and premalignant cases in present study was 48.2% (Table 7) which is comparable with Naik et al[11] 49% and Tyagi et al[31] 58.5%. Other studies were Gredmark et al[16] 15%, Lee et al[12] 25.8% and Cheema et[2] al 30%. The ratio of cervical to uterine cancer was 2.9:1 similar to Tyagi et al[31] 2.6:1 and Lee et al[12] it was 1.2:1. Cervical cancer was responsible for 33% of PMB, squamous cell carcinoma was the most common cancer (25.9%). (Fig. 2)

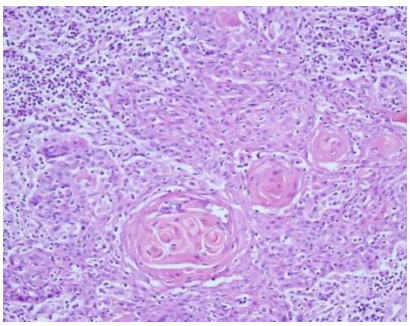

Fig. 2: Well differentiated Squamous cell carcinoma of cervix (H&E x40x)

Table 7: Incidence of malignant tumors in case of postmenopausal bleeding

Study	Malignant lesions
Gredmark et al	15
Lee et al	25.8
Naik et al	49.1
Cheema et al	30.0
Tyagi et al	58.5
Present Study	48.2

Hence cervical cancer is almost thrice as common as endometrial cancer in our study of women with postmenopausal bleeding. These results support the fact that the diagnostic focus in our country with history of PMB should be towards excluding cervical pathology.

In this study endometrial adenocarcinoma is the most common (9.2%) cause of PMB after cervical carcinoma which was similar to Naik et al[11] 9.6%. Other studies were Gredmark et al[16] 8%, Cheema et al[2] 10%, Lee et al[12] 11%, Tyagi et al[31]13%. Histologically 12 cases (7.4%) were there of adenocarcinoma in which 9 (5.4%) were endometrioid adenocarcinoma, 2 cases (1.2%) were papillary serous adenocarcinoma and 1(0.6%) case was endometriod carcinoma with mucinous differentiation. Also reported was one case of MMMT (0.6%). (Fig. 3)

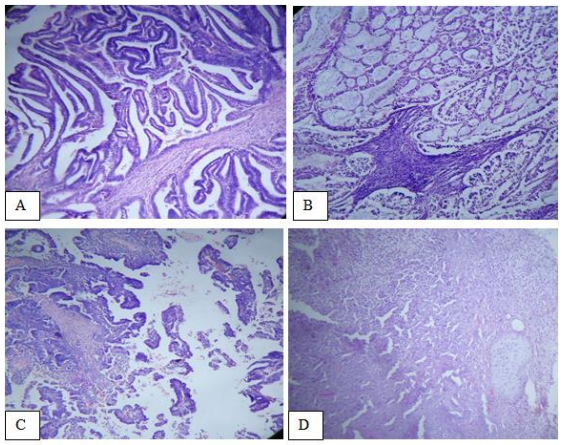

Fig. 3: Endometrial carcinoma.
A: Endometrioid carcinoma.
B: Endometrioid carcinoma with mucinous differentiation.
C: Papillaryserous carcinoma.
D: Malignant mixed mullerian tumor (H&Ex 10x)

Simple endometrial hyperplasia was observed in 11 cases (6.7%), 3 cases were endometrial hyperplasia with atypia (1.85%). Hyperplasia is significant that it carries the risk of development of endometrial cancer more so with hyperplasia with atypia. Other studies were 3-13%.[2,11,12,16]

Conclusion

PMB is a symptom which should not be taken lightly. Accurate diagnosis is usually made by histopathological examination. In our study, a wide spectrum of both neoplastic and non- neoplastic conditions of female genital tract has displayed as a cause of PMB with predominance of benign causes (51.6%). The main aim of evaluation of PMB is to exclude premalignant and malignant lesions. Cervical cancer is still the most common cause of PMB, which point out that the effective implementation of screening program is utmost important. More awareness among people, especially elderly women should be made about the importance of pap screening.

PMB indicates malignancy until proved otherwise and it demands thorough evaluation of patients with histopathological confirmation. An accurate diagnosis is immensely important as it will be helpful for the management of patient by implementing a proper treatment plan.

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