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Original Research Article

Endometrial pathology in postmenopausal women: Analysis of 112 cases in tertiary care centre

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ABSTRACT

Background: Postmenopausal bleeding is a frequent finding accounting for 5-10% of women in gynaecology clinic. About 10% of these patients have primary or secondary malignancy.
Aim: The histopathological patterns of endometrium, in postmenopausal women presenting with bleeding were studied along with the frequency of endometrial cancer.
Materials and Methods: It was both a prospective and retrospective, observational study carried out over a period of one and half year in tertiary care teaching hospital on 112 postmenopausal women, above 40 year of age with history of one year of amenorrhoea without hormone replacement therapy. The samples were obtained by dilatation and curettage and endometrial pipelle procedure.
Results and Discussion: Maximum patients belonged to age group of 46-50 year. The most common histopathological pattern observed was atrophic endometrium in 42 (37.5%) patients followed by simple hyperplasia in 13(11.6%) and endometrial polyp in 7(6.25%) cases. Irregular shedding of endometrium was diagnosed in 8 case (7.14%). The maximum patients of endometrial carcinoma (5.35 %) were noted in 61-65 age groups. Inflammatory pathology was found in 4(3.56%) and atypical hyperplasia was seen a single case (0.89%). In 8 cases, the opinion could not be offered due to inadequacy of sample.
Conclusion: As the incidence of malignancy in postmenopausal period remains sufficiently high, it requires immediate investigation in the form of endometrial sampling for early diagnosis, prompt treatment and vigilant follow up.

1. Introduction

Postmenopausal bleeding (PMB) is defined as any bleeding from the genital tract with a history of one year of amenorrhea and not receiving any hormone replacement therapy (HRT). It is often associated with benign conditions but there is 10% risk of having genital malignancies such as cervical, endometrial, vaginal, ovarian, and vulval cancers.[1] Endometrial cancer present earliest with warning symptom of PMB, which provokes women to seek medical help and getting detected at early stages of endometrial cancerwhichcan improve the chances of cure rate and therefore reduces mortality.[2] The most commonly used technology for evaluation of endometrium are transvaginal ultrasound (TVS), hysteroscopy, endometrial biopsy by pipelle, dilatation and curettage. Tissue examination is considered as gold standard for the diagnosis.[3] Here we studied various histopathological patterns of endometrium, in postmenopausal women presenting with postmenopausal bleeding along with the frequency of endometrial cancer.

2. Materials and Methods

This study was undertaken in tertiary care teaching hospital in postmenopausal women presented with postmenopausal bleeding. It was both prospective and retrospective observational study carried out over a period of one and half year and their histopathological patterns were examined. The patients above 40 yrs. of age with one year history of amenorrhoea without prior history of hormone

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replacement therapy were included irrespective of their parity, social background and previous medical, surgical or gynaecological history.

The patient with abnormal uterine bleeding in women less than 40 yrs of age, uterine bleeding due to intrauterine devices and related complications were excluded. Chemotherapy, radiation induced menopause and patient on hormone replacement therapy were excluded from study. The specimens considered for histopathological study comprised of endometrial biopsy by dilation and curettage and endometrial pipelle procedures done for diagnostic or therapeutic purposes. Endometrial tissue was fixed immediately in 10% buffered formalin and further processed. The paraffin embedded tissues were sectioned at 4-5 μ and then stained with hematoxylin and eosin. Histopathological examination was done taking into consideration patient's clinical details and ultrasonographic findings. Slides were evaluated by two pathologist in a blinded fashion.

3. Results

Total 112 consecutive women who met with the inclusion criteria were included in study. Maximum females belonged to age group of 46-50 year followed by 41-45 year while the mean age was 51.79 year. Youngest patient was 41 year while oldest patient was 80 year.

Table 1: Age incidence of PMB in postmenopausal women

Age Group (Year)	Number	Percentage
41-45	26	23.21
46-50	39	34.82
51-55	19	16.96
56-60	14	12.5
61-65	10	8.92
>65	4	3.57
Total	112	100

Apart from postmenopausal bleeding, the commonest associated symptoms were vaginal discharge, pain in lower abdomen and low backache. Dilatation and curettage was the most common endometrial sampling method used in 82 patients (73.21) followed by endometrial biopsy by pipelle method in 30 patients (26.79%)

Inflammatory pathology was found in 4 patients (3.56%). Out of which acute endometritis seen in 2 patients, each of them was of 61yrs old. A single case of chronic endometritis was seen in 45 year patient and xanthogranulomatous endometritis in 1 patient who presented clinically as pyometra. [Figure 1a,b]

The most common histopathological pattern observed was atrophic endometrium seen in 42 patients (37.5%) with mean age of 52 yrs. followed by Proliferative endometrium in 18 patients (16.07%) and secretory endometrium in 5 patients (4.46%). Hyperplasia was seen in 14 patients (12.49%). The Benign hyperplasia was noted in 13 cases (11.6%) with mean age of 56 yrs, while single case of atypical hyperplasia was found (0.89%) in 65 year [Figure 2 a,b]. Irregular shedding of endometrium was diagnosed in 8 patients (7.14%). The Endometrial polyp was seen in 7 cases with mean age of 52 yrs. All these cases were correlated radiologically. The maximum cases of endometrial carcinoma that constitutes 5.35 % were seen in 61-65 age group. The youngest patient of endometrial carcinoma was 50 year while oldest was 76 year. Out of total 6 cases of endometrial, 4 had history of diabetes and one had hypertension. In 4 cases type I endometrial carcinoma was diagnosed [Figure 3a,b] while in 2 patients diagnosis of type II endometrial carcinoma was given [Figure 4a,b]. On 8 biopsy specimens, opinion could not be rendered as the samples were insufficient for interpretation due to scanty endometrial tissue.

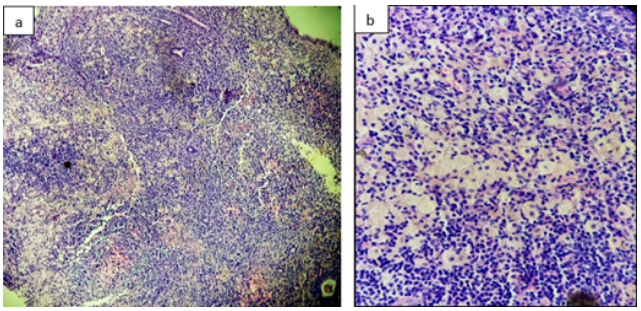

Fig. 1: a: Xanthogranulomatous endometritis: Replacement ofendometrium by sheets of histiocytes admixed with lymphocytes and plasma cells (H&E, 10X), **b:**Xanthogranulomatous endometritis- The foamy nature of histiocytes wellappreciated (H&E, 40X)

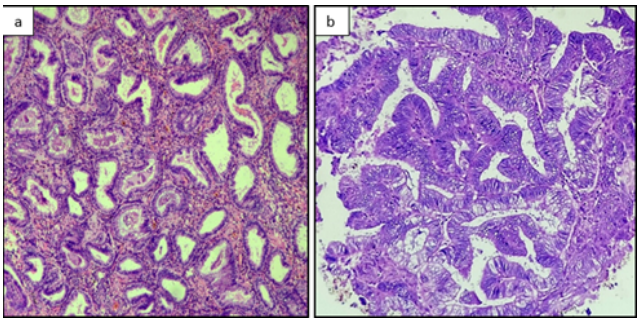

Fig. 2: a: Simple Hyperplasia -The gland to stroma ratiois increased, endometrial glands irregular in size and shape without evidence of cytological atypia(H&E 10X), Figure **b:** Atypicalendometrial hyperplasia endometrial glands arranged back to back withlittle intervening stroma.The glands show architectural and cytological atypia (H&E20X)

Table 2: Distribution of cases as per Histopathology Diagnosis

S. No	Histopathology Diagnosis	Number	Percentage
1	Atrophic Endometrium	42	37.5
2	Proliferative Phase	18	16.07
3	Non atypical endometrial hyperplasia (simple hyperplasia)	13	11.6
4	Irregular shedding	8	7.14
5	Endometrium Polyp	7	6.25
6	Endomerial Adenocarcinoma	6	5.35
7	Secretary Phase	5	4.46
8	Acute Endometritis	2	1.78
9	Chronic Endometritis	1	0.89
10	Xanthogranulomatous Endometritis	1	0.89
11	Atypical endometrial hyperplasia	1	0.89
12	Inadequate	8	7.14
	Total	112	100

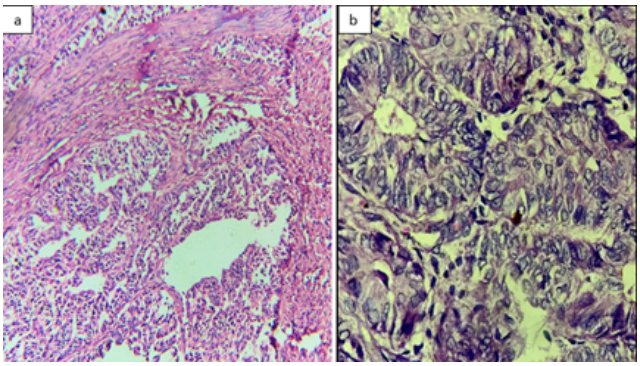

Fig. 3: a: Endometrialcarcinoma Type I: compactly arranged endometrial glands having architecturaland cytological atypia with invasion in underlying myometrium (H&E, 10X), **b:** The glands lined by columnar cells showing pseudostratification, nucleomegalypleomorphism and coarse chromatin (H&E 40X)

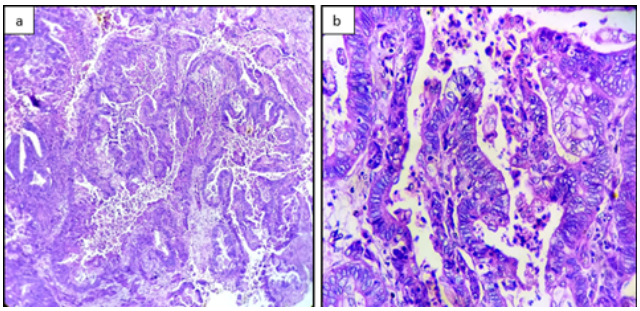

Fig. 4: a: Endometrial Carcinoma type II: Tumour showing papillary architecture, **b:** Papillae lined by columnarcells showing marked cytologic atypia, high N:Cratio, pleomorphism and mitotic figures.The core of the papillae shows neutrophilic infiltrate. (H&E, 40X)

4. Discussion

Endometrium reflects hormonal status in a female with abnormal uterine bleeding. Postmenopausal bleeding is considered as abnormal and needs investigation.[4,5] The incidence of premalignant and malignant endometrial disorders increases in the postmenopausal age group. Although vaginal bleeding is the most common symptom, patients may present with leucorrhoea, post-coital bleeding or spotting and pelvic pain, or may even have asymptomatic course.[6] The Postmenopausal bleeding may be a one of the manifestation of organic endometrial pathologies such as endometrial polyp, hyperplasia or carcinoma or may be of included in unexplained category if no obvious pathology is detected.[7,8] The endometrial evaluation method includes various modalities such as transvaginal sonography, hysteroscopy, endometrial biopsy, biopsy by pipelle, dilatation and curettage. Computed tomography and magnetic resonance imaging can also be used to arrive at a preoperative diagnosis while histopathology serves as the gold standard for definitive diagnosis. Endometrial sampling is essential to exclude endometrial carcinoma. Accurate and precise histological diagnosis is mandatory as the treatment modality differs in benign and malignant category. Surgical treatment is often required for premalignant or malignant endometrial diseases and exorbitant treatment can thus be avoided if diagnosed at early stage.[6,9] The most common age group of patients with postmenopausal bleeding was 46-50 year with the range of 41 to 80yrs. The youngest patient was 41 yrs while oldest patient was of 80 year.[10] Atrophic Vaginitis was the most common abnormality seen in 42 patients (37.5%) followed by proliferaive endometrium in 18 (16.07%). The atrophic endomerium is the result of ovarian failure, on histology displays shows endometrial glands which are simple, tubular, cystic which are neither proliferative nor secretory embedded in a fibrous endometrial stroma.[11,12] Irregular shedding was seen in 8 cases (7.14%). It is due to slow

degeneration of the corpus luteum and prolonged exposure of menstruating endometrium to the waning progesterone. Clinically, it manifests by cyclic prolonged menstruation and on histology is characterised by mixed pattern with both proliferative and secretory type of endometrium.[13] The inflammatory pathology was noted in 4 patients. Acute endometritis is usually observed with history of abortion, in postpartum state or with instrumentation and is characterised by presence of neutrophil clusters in the endometrial stroma and within uterine glands. In our cases we could not procure any such history of instrumentation. Chronic endometritis characterised by presence of lymphocytes and plasma cells in the endometrial stroma and glands. Xanthogranulomatous endometritis reveals replacement of the endometrium by sheets of lipid containing foamy histiocytes admixed with chronic inflammatory cells comprised oflymphocyes and plasma cells. This infiltrate is seen surrrounding the distorted and atrophic glands. It is mostly seen in patient with hematometra which is observed in our case.[14] Endometrial polyps are common, with their prevalence appearing to increase with age. In postmenopausal women, estrogen receptors are more prevalent in polyps than the adjacent normal endometrium, which may alter proliferative process, resulting in polyp formation. In present study they occupy 6.25% cases. The microscopic appearance consists mixture of dense fibrous tissue (stroma), large and thick-walled vascular channels, and glandular spaces of varying shapes and sizes, covered by a surface epithelium. Most endometrial polyps are benign but the risk of malignancy is highest in postmenopausal women with vaginal bleeding (2.3%).[3] Non atypical endometrial hyperplasia (benign hyperplasia) was seen in 13 patients (11.6%), atypical endometrial hyperplasia was seen in 1 patient (0.89%). It is important to diagnose hyperplasia because they are considered to be the precursor lesions of endometrial carcinoma. The overall risk of progression of hyperplasia to cancer is 5-10%.[10] In simple (non atypical) hyperplasia there is an increase in gland to stroma ratio. Although there is back to back arrangement of glands focally, the intervening stroma is usually retained. These lesions reflect an endometrial response to persistent estrogen stimulation and rarely progresss to adenocarcinoma. Atypical endometrial hyperplasia is composed of complex patterns of proliferating glands displaying nuclear atypia seen as nucleomegaly, pleomorphism and mitosis. These glands are more back to back with very little intervening stroma and often have complex outlines due to branching structures.[15]Diagnosis ofAtypical endometrial hyperplasia is important as treatment options differ significantly in simple versus atypical hyperplasia. The simple hyperplasia is usually treated conservatively (normalization of the cycle through weight loss, metformin; oral contraceptives; cyclical gestagens; (gestagen IUD). Preventive hysterectomy is done only in exceptional cases (e.g., extreme obesity without any prospect of weight loss. The surgery should be done as a total hysterectomy and it must include removal of the cervix. The treatment of atypical hyperplasia / endometrioid intraepithelial neoplasia generally consists of total (not supracervical) hysterectomy. Conservative treatment with high-dose gestagens and close histological monitoring should only be considered in exceptional cases when the patient wants to preserve the fertility.[16] In present study, 6% of total cases belonged to endometrial carcinoma which belonged age group of 51-55.[17] Postmenopausal bleeding is the most common presentation of endometrial carcinoma. Approximately 80% of them develops in the postmenopausal period.[18,19] Type IEndometrial carcinoma was predominant histological type observed in our study similar observations were made by other authors.[20] The median age at diagnosis of Endometrial Carcinoma is the sixth decade, although 20% to 25% of the cases will be diagnosed premenopausally.[21] The endometrial carcinoma is classified into two types: Type 1 is more common accounting for of 70–80% cases, consist of endometrioid, , diploid, hormone-receptor positive tumours that are moderately or well-differentiated and more common in obese women. Patients presenting with Type 1 tumours tend to have localized disease confined to uterus and have a favourable prognosis. In contrast, Type 2 tumours constitute of 20–30% cases that are more common in non-obese women. They display aneuploid, non endometriod, high grade, poorly differentiated morphology, hormone receptor status with high risk of metastasis and poor prognosis. Type 1 endometrial type is characterised by well defined glands lined by cytologically malignant columnar epithelial cells. These tumours exhibit enlarged stratified nuclei, but degree of nuclear pleomorphism is mild. Type II endometrial carcinoma is characterised by malignant cells with serous type of morphology characterised by marked cytological atypia including high N: C ratio, hyperchromasia and atypical mitotic figures.[22] Treatment modalities include - Surgery which involves hysterectomy with bilateral salpingo-oophorectomy with or without lymph node dissection and omentectomy with several safe options in surgical approach. Extent of staging may vary according to the patient age, comorbidities, tumor histology, its grade, disease distribution, surgeon preference and institutional practice. Surgery alone is typically sufficient to cure early-stage endometrial carcinoma, however, it is recognized that tumours with ‘high-risk’ features have a high likelihood of recurrence and adjuvant treatment (radiation and/or chemotherapy) is recommended.[23]

5. Limitation of the study

In Retrospective analysis of cases, complete clinical details including ultrasonographic features could not be procured

in some cases therefore endometrial thickness couldnot be correlated with histopathology. So also in 8 cases, sample was inadequate and advantage of repeat procedure could not be availed.

6. Conclusion

In our study, the prevalence of endometrial carcinoma was 5.35% . Although major proportion of pathological lesions are benign, significant number of cases belong to atypical endometrial hyperplasia and malignancy . The early detection of atypical hyperplasia and endometrial carcinoma in postmenopausal woman helps the gynaecologist to plan definitive treatment modalities.

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8. Conflict of Interest

The authors declare they have no conflict of interest.

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