THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (January–February 2016) 66(1):42–46
DOI 10.1007/s13224-014-0627-z

ORIGINAL ARTICLE

Correlation of Endometrial Thickness with the Histopathological Pattern of Endometrium in Postmenopausal Bleeding

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Received: 16 January 2014 / Accepted: 22 September 2014 / Published online: 4 November 2014

About the Author

Dr. Pushpa Singh was born on August 10, 1954. She completed her graduation and postgraduation from GRMC, Jivaji University, Gwalior. She did her residency and worked as a scientific pool officer from 1980 to 1986 in SKH and LHMC, New Delhi. She joined Central Health Services in 1987 in Dr. R.M.L. Hospital, New Delhi. She is presently working as Professor and Head of the Department of Obstetrics and Gynecology since 2004. She has published 30 articles in national and international publications and has various presentations. She has contributed a chapter in a Gynecology textbook by Dr. Salan on primary carcinoma of fallopian tube. Her main interest lies in high risk obstetrics and oncology. The study was a prospective study conducted in the Department of Obstetrics and Gynecology, PGIMER, Dr. Ram Manohar Lohia Hospital, New Delhi between 2010 and 2011. The study was approved by the institutional ethical and research review board

Abstract

Background Menopause is the permanent cessation of menstruation resulting from the loss of ovarian follicular activity. Bleeding that occurs 12 months after the last menstrual period is labeled as postmenopausal bleeding.

Aims & objectives The aim of the present study was to study endometrial thickness by transvaginal sonography, and correlate it with the cytological pattern evaluated by endometrial aspiration and histopathological pattern of the hysteroscopic directed biopsy.

Results Sixty patients presenting with postmenopausal bleeding in outpatient department, after applying both inclusion and exclusion criteria, were enrolled in the present study. Majority (38.33 %) of patients had atrophic endometrium or normal endometrium. Endometrium was hyperplastic in 18 (30 %) patients, polyp in 6 (10 %) patients, and growth in 7 (11.67 %) patients. On histopathology, majority of patients (38.33 %) had atrophic endometrium. Endometrial hyperplasia was detected in 14 (23.33 %) out of which 11 had simple hyperplasia while 3 had atypical hyperplasia. Endometrial cancer was detected in 8 (13.33 %) patients. Out of 8 cases of endometrial malignancy, one case was confirmed as endometrial adenocarcinoma on histopathology.

Conclusion Role of endometrial thickness cannot be undermined for detecting patients at high risk especially with comorbid conditions. Histo-pathological evaluation is mandatory for ruling out malignancy in selected cases of PMB through hysteroscopy.

Keywords Histological pattern of endometrium

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Introduction

Menopause is the permanent cessation of menstruation resulting from the loss of ovarian follicular activity [1]. Bleeding that occurs 12 months after the last menstrual period is labeled as postmenopausal bleeding (PMB). Approximately, 3 % of menopausal women suffer from this condition and require prompt and thorough evaluation. The primary aim was to rule out endometrial pathology (carcinoma and atypical hyperplasia). Potential screening modalities for endometrial cancer include transvaginal sonography (TVS), saline infusion sonohysterography, 3-D color doppler ultrasound, endometrial sampling through endometrial aspiration biopsy, dilatation and curettage, hysteroscopy, and guided biopsy. In the present study, non-invasive TVS, the minimally invasive technique endometrial aspiration, and hysteroscopy have been used for the evaluation of endometrial pathology in patients with PMB. Subsequently, an attempt has been made to effectively and promptly evaluate a woman with PMB.

Aims and Objectives

The aim of the present study was to study endometrial thickness by transvaginal sonography and correlate it with the cytological pattern evaluated by endometrial aspiration and histopathological pattern of the hysteroscopic directed biopsy.

Materials and Methods

The present study was a prospective study conducted in the department of Obstetrics and Gynecology, PGIMER, Dr. Ram Manohar Lohiya hospital, New Delhi. A total of 60 patients were included in this study who presented with postmenopausal bleeding or spotting. The study was approved by the institutional ethical and research review board. Inclusion criteria included patients with postmenopausal bleeding. Exclusion criteria included patients with vaginal infection, premalignant and malignant lesions of vagina, vulva and cervix, cervical and endocervical pathology, bleeding disorders, adenexal masses, patients on tamoxifen and hormonal therapy. After history, detailed clinical examination, and routine investigations, all patients were subjected to Pap smear and endometrial aspiration for histopathological examination. This was preceded by transvaginal sonography. The characters that were studied on TVS included endometrial thickness, echogenicity of endometrium, uterine size, uterine cavity, cervical canal, myometrium, any uterine growth/polyp, any fluid in endometrial cavity and bilateral adenexae. The endometrium and uterine cavity were considered normal if transvaginal sonography showed a hyperechoic line in middle of the uterus with a homogenous endometrial lining with distinct margins. All other findings such as deformity of endometrial lining, absence or disturbed central hyperechoic line, any solid cystic appearance, any fibroid, growth or polyp with or without well-defined margins. Endometrial cancer was suspected in presence of heterogenous endometrium with irregular interface between endometrium and myometrium with or without fluid collection. In invasive uterine cancer, subendometrial halo is lost. The intrauterine cavity was seen for any intracavitary collection. The findings were noted, and the patients were scheduled for hysteroscopy and biopsy after pre-anesthetic checkup. Hysteroscopy was performed with HOPKINS II straight forward 4 mm, 0 degree-telescope (KARL STORZ, GERMANY). The overall observation was made of shape of uterine cavity, endometrial appearance, and presence of any foreign body, synechiae, polyp, any growth, and submucous fibroids. Uterine mucosa appeared smooth, pink, or pale in case of atrophic endometrium. If normal, biopsy was taken from anterior, posterior, two side walls along with fundus in one vial and sent for histopathological examination. If abnormal, biopsy was taken from suspicious area, and polypectomy was done if it was present. The histopathology report was divided into 6 groups that were atrophic endometrium/inconclusive report, hormonal effect, endometrial polyp/fibroid, hyperplastic endometrium, disordered proliferative, and endometrial carcinoma. All the above data were compiled and statistically analyzed using starview4.5 (Berkely, California) and IBM-SPSS Statistics v19.0.0 Multilingual. Data were compared using Chi-squared test and Fischer exact test with a two-tailed P value <0.05 being considered as significant.

Observations and Results

Sixty patients presenting with postmenopausal bleeding in outpatient department, after applying both inclusion and exclusion criteria, were enrolled in present study. Majority (20) of the patients (33.33 %) were in age group of 45–50 years. Majority of the cases (35 %) had 3 children. Nulliparity was observed in 5 % of cases. The majority (36) of patients had BMI of less than 24. Only 12 % had BMI >28. Majority of patients (27 %) attained menopause between 45 and 50 years. Twenty patients were diabetic and 23 were hypertensive. The mean endometrial thickness on TVS was 5.76 ± 3.3877 mm with a range of 2.2–18 mm (Table 1). Majority of patients (40 %) had ET < 4 mm. 6 patients had ET >10 mm. Majority (38.33 %) of patients had atrophic endometrium or normal

Table 1 Distribution of cases according to endometrial thickness on transvaginal sonography

ET (range in mm)	No. of cases	Percentage (%)
≥4	24	40
4.1–6	13	21.67
6.1–8	8	13.33
8.1–10	9	15
>10	6	10
Total	60	100

The mean ET was 5.76 ± 3.3877 mm with a range of 2.2–18 mm

Table 2 Distribution of cases according to histopathology

Histology	No. of cases	Percentage (%)
Normal	6	10.0
Atrophic	23	38.33
Disordered	7	11.67
Endometrial polyp	2	3.33
Hyperplasia		
Simple	11	18.33
Atypical	3	5.0
Carcinoma	8	13.33
Total	60	100

endometrium. On hysteroscopy, endometrium was hyperplastic in 18 (30 %) patients, polyp in 6 (10 %) patients, and growth in 7 (11.67 %) patients. On histopathology, majority of patients (38.33 %) had atrophic endometrium (Table 2). Endometrial hyperplasia was detected in 14 (23.33 %) out of which 11 had simple hyperplasia while 3 had atypical hyperplasia. Endometrial cancer was detected in 8 (13.33 %) patients. Out of 8 cases of endometrial malignancy, one case was confirmed as endometrial adenocarcinoma on histopathology after polypectomy through hysteroscope. In patients with normal and atrophic histology, majority had ET <4 mm those with hyperplasia had ET >4 mm and with polyp had ET >6 mm. No case of polyp and endometrial cancer was diagnosed at ET <6 mm, while 3 cases of hyperplasia were missed at a cut-off of 4 mm of ET (Table 3). Statistical analysis revealed *P* value <0.0001 for ET at 4 mm and 6 mm which is highly significant (Table 4). Twenty-three patients with atrophic findings on hysteroscopy had a mean ET of 3.48 mm, those with normal findings had mean ET of 4.05 mm. Patients showing hyperplastic endometrium had mean ET of 5.81 mm and polyp of 7.8 mm. Seven patients had abnormal growth on hysteroscopy suggestive of malignancy and had mean ET of 12.1 mm. The sensitivity of hysteroscopy as compared to histopathological examination for postmenopausal women with PMB is 96.77 %, and specificity is 96.55 %. The PPV of hysteroscopy as compared to histopathology is 96.77 %, and NPV is 96.55 % with diagnostic accuracy of 96.66 %. On application of chi-square test, the *p* value is <0.0001, which is extremely statistically significant. Thus, the diagnostic accuracy of hysteroscopy with respect to histopathology is highly significant (Figs. 1, 2, 3, 4).

Discussion

The incidence of postmenopausal bleeding decreases with increasing age while the probability of cancer as the underlying cause increases. The prevalence of endometrial cancer in women with PMB is 3–10 %.The risk of endometrial cancer in women with PMB increases with age approximately 1 % at the age of 50 years to 25 % at 80 years of age. Traditional dilatation and curettage is now being replaced by other techniques like miniature endometrial biopsy devices, TVS to measure ET and hysteroscopy and directed biopsy. Present study was undertaken to evaluate how best a patient with PMB can be investigated by non-invasive or minimally invasive techniques. In present study, the sensitivity and specificity of TVS for suspecting endometrial pathology at ET ≤ 4 mm were 87.09 and 75.86 %, respectively. Similar studies conducted by different investigators, Karlsson et al. [2], Gull et al. [3], Garuti et al. [4] , Tinelli et al. [5], and Kaur et al. [6], had shown the sensitivity ranging from 89 to 100 % while specificity from 54.8 to 86 % at ET of 4 mm. In the present study, sensitivity, specificity, PPV, and NPV for

Table 3 Comparison of endometrial thickness with histopathology

Histology	No. of cases	Endometrial thickness on TVS (in mm)				
		≤4	4.1–6	6.1–8	8.1–10	>10.1
Normal	6	5	0	1	0	0
Atrophic	23	17	5	1	0	0
Disordered	7	1	4	2	0	0
Endometrial polyp	2	0	0	1	1	0
Hyperplasia	14	3	4	3	3	1
Malignancy	8	0	0	1	1	6

Table 4 Diagnostic values of TVS at ET of 4 and 6 mm

	ET on TVS (in mm)	
	≤4	≤6
Sensitivity	87.09 %	61.29 %
Specificity	75.86 %	93.10 %
PPV	79.41 %	90.47 %
NPV	84.61 %	69.23 %
Positive LR	3.60	8.88
Negative LR	0.17	0.41
Diagnostic accuracy	81.66 %	76.66 %
P value	<0.0001	<0.0001

Statistical analysis revealed *P* value <0.0001 for ET at 4 and 6 mm which is highly significant

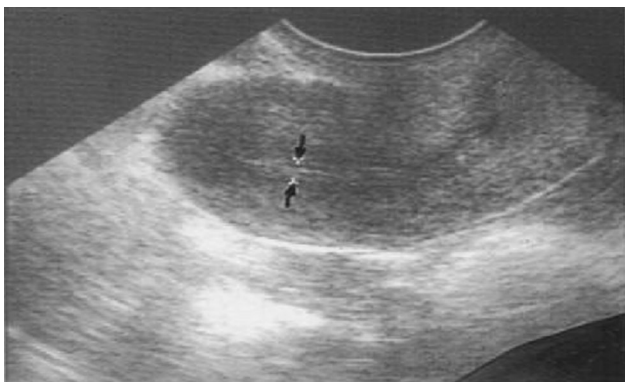

Fig. 1 Sagittal transvaginal ultrasound image demonstrates correct placement of calipers for endometrial thickness measurement (*arrows*) in a postmenopausal woman

Fig. 2 Image shows diffuse thickening due to endometrial hyperplasia. The finding was confirmed at biopsy

hysteroscopy in detecting endometrial pathology were 96.77, 96.55, 96.77, and 96.55 %, respectively, with diagnostic accuracy of 96.66 %. These statistical results correlate with those by Garuti et al. [4], Loverro et al. [7],

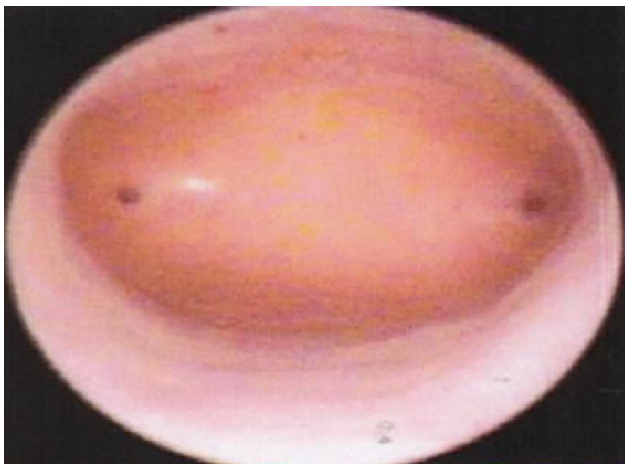

Fig. 3 Hysteroscopic view of atrophic endometrium in a patient with PMB

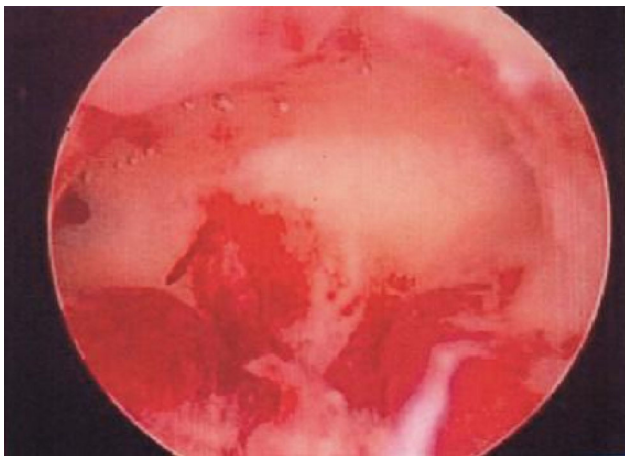

Fig. 4 Hysteroscopic examination showing hyperplastic and hyperemic endometrium in a 70-year female with ET of 10 mm on TVS, which was confirmed as atypical hyperplasia on histology

and Tinelli et al. [5]. In the present study, benign pathology (normal, atrophic, polyp, myoma) was diagnosed in 51.66 % out of which majority had atrophic endometrium. Endometrial cancer was detected in 8 (13.33 %) patients. Out of 8 cases of endometrial malignancy, one case was confirmed as endometrial adenocarcinoma on histopathology after polypectomy through hysteroscope. Similar incidences have been reported in studies of Karlsson et al. [2], Gerber et al. [8], and Kaur et al. [6]. Thus, all patients with PMB need preliminary evaluation by TVS for ET and endometrial sampling to rule out premalignant and malignant pathology as early as possible. Conduction of hysteroscopy to the diagnostic armamentarium of gynecologist has definitely been beneficial in early diagnosis and treatment in women with PMB. Hysteroscopic guide biopsy can help further evaluation and to guide the choice of treatment in women with PMB.

Conclusion

Evaluation of PMB at the earliest is essential for diagnosing endometrial status for early intervention. Role of endometrial thickness cannot be undermined for detecting patients at high risk especially with comorbid conditions. Histopathological evaluation is mandatory for ruling out malignancy in selected cases of PMB through hysteroscopy. Hysteroscopy can be considered as a first line modality in the management of high risk patients with PMB.

Compliance with ethical requirements and Conflict of interest The study was approved by the institutional ethical and research review board. There is no conflict of interest.

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