



Analysis of the Reasons for Postmenopausal Bleeding that Originated from the Uterus

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ABSTRACT

Objective: We aimed to analyze the reasons for postmenopausal bleeding that originated from the uterus in cases who consulted our menopausal clinic.

Methods: Sixty-eight patients who visited the Gaziosmanpaşa Taksim Training and Research Hospital menopausal clinic with the complaint of postmenopausal bleeding were included in this prospective study. Systematic and gynecological examinations were conducted on these patients when they first visited. The age of the patients, last menstruation dates, characteristics of the vaginal bleeding, whether the patients had undergone hormone replacement treatment or not, number of pregnancies, whether they had a systematic disease or not, and alcohol consumption and smoking were investigated and recorded. Patients who had uterine bleeding that originated from the vagina and that was related to a systematic disease were excluded. The patients' vagina and vulva were examined, with the patient in the dorsolithotomy position on the gynecological table. Each patient underwent a smear test, followed by a transvaginal ultrasound.

Results: The average age of the 68 patients who were included was 57 years, with the youngest aged 45 years and the oldest aged 83 years. As a result of the sampling done with these 68 patients, endometrium cancer was observed in six of them, with three of them aged over 65 years. In our study, 8.8% patients were detected with endometrium cancer. There are six nullipara patients according to the number of births and four of them were diagnosed with endometrium cancer. The menopause period of five of these six patients who were diagnosed with endometrium cancer was over 10 years. For the other reasons of postmenopausal bleeding, it was detected that atrophy in our series was 41.2%, hyperplasia was 7.4%, polyp was 35.3%, submucous myoma was 2.9%, cervical cancer was 2.9%, and cervical intraepithelial neoplasia-2 was 1.5%. In one of the cases who was diagnosed with endometrium cancer, the thickness of the endometrium was detected as 11 mm, and in the rest of the cases, this thickness was 20 mm.

Conclusion: Beside obviously seeing the benefit of getting a prior knowledge for the patients about the endometrium by detecting the thickness of the endometrium by conducting transvaginal ultrasonography on the patients who have postmenopausal bleeding, in the postmenopausal bleeding, endometrial curettage is the golden standard. (*JAREM 2016; 6: 78-83*)

Keywords: Uterine bleeding, postmenopausal bleeding, endometrial curettage, Endometrium cancer

INTRODUCTION

Menopause is a natural event of the normal aging process in which menstruation permanently stops because of the loss of ovarian functions. The postmenopausal period is the relative ovarian quiescence following menopause. Postmenopausal uterine bleeding is an important finding that can occur within one or several years after menopause. Although postmenopausal bleeding often results from endometrial polyp, leiomyoma, hyperplasia, and atrophic endometrium, it can be the first sign of endometrial carcinoma in 10% of patients. Therefore, the main goal of investigating postmenopausal bleeding in women is to rule out severe intrauterine pathologies, particularly endometrial carcinoma. The conventional procedure of postmenopausal bleeding investigation is cervical dilatation and curettage (D&C).

In this study, we aimed to analyze the uterine-related causes of postmenopausal bleeding in patients who visited our menopausal clinic.

METHODS

This randomized controlled prospective study included 68 patients admitted with the complaint of postmenopausal bleeding to the menopausal clinic of Gaziosmanpaşa Taksim Training and Research Hospital in 2009. Patients having amenorrhea for one or more years were accepted to be in the menopausal period. At the time of admission, the patients underwent a general systematic and gynecological examination. Ethical approval was obtained from the Ethics Committee of the Education and Planning Board of Gaziosmanpaşa Taksim Training and Research Hospital. All the patients were informed about the procedures that they would undergo, and their verbal informed consent was obtained. The ages, last menstruation dates, and vaginal bleeding characteristics of the patients; whether the patients had received hormone replacement treatment; number of pregnancies; presence of systematic disease; smoking habits; and alcohol consumption were questioned and recorded. Patients with uterine bleeding that originated from the vagina and that was associated with a



systematic disease were excluded from the study. Only two hypothyroidism cases were included in the study (one had endometrial hyperplasia and the other had endometrial polyp).

The patients were placed in the dorsolithotomy position on the gynecological table, and their vulvas and vaginas were inspected. PAP smear tests were performed. The smears were evaluated by pathologists using the Bethesda system. Transvaginal ultrasound was performed in the dorsolithotomy position with an empty bladder after the patient urinated.

The probe was inserted in the vagina, cervix, cervical canal, and contours of the endometrial cavity. The ovaries were evaluated by taking coronal and sagittal sections. A normal endometrium and uterine cavity were accepted as a homogeneous and hyper-echoic line separated from the myometrium with apparent margins in the middle of the uterus. Any discontinuance, deformation in the endometrial line, lack of intense central echo line, or structure with apparent or non-apparent margins with a different echo and intensity were accepted as abnormal. Both the ovaries were assessed in terms of pathologies. For histopathological evaluation, the cervix was cleansed with povidone-iodine and grasped with a tenaculum. D&C was applied. The material was sent to the pathology laboratory of our hospital. The patients whose smear results revealed high-grade squamous intraepithelial lesions (HSIL) and atypical squamous cells—cannot exclude

high-grade squamous intraepithelial lesion (ASC-H) underwent cervical biopsies with the guidance of colposcopy.

Statistical Analysis

The data were analyzed using SPSS (Statistical Package for the Social Sciences Inc., Chicago, IL, USA) software. Statistical analysis results were presented as mean± standard deviation (M±SD) and percentage values.

RESULTS

The mean age of the 68 patients included in the study was 57 years. The youngest age was 45 years and the oldest was 83 years. The demographic features of the patients are given in Table 1. In the sampling of 68 patients, endometrial cancer was found in 6 cases, and 3 of these patients were over 65 years old. There were 6 nulliparous patients, and 4 of these were diagnosed with endometrial cancer. The duration of menopause was less than 5 years in 41.2% of the patients, between 5 and 10 years in 26.5% of the patients, and greater than 10 years in 32.4% of the patients. The menopause duration was greater than 10 years in 5 of the 6 patients diagnosed with endometrial cancer. Considering body mass index (BMI), obese patients constituted 83% of our case group, and 4 of these were diagnosed with endometrial cancer. One patient was accepted to be thin, and she was also diagnosed with endometrial cancer.

Table 1. Demographic features of patients included in the study

		Number	Percentage	Cumulative percentage
Age	45-54	32	47	47.1
	55-64	22	32.4	79.4
	>65	14	20.6	100.0
	Total	68	100.0	
		Number	Percentage	Cumulative percentage
Parity	Nulliparous	6	8.8	8.8
	Primiparous	4	5.9	14.7
	Multiparous	38	55.9	70.6
Duration of menopause	Grandmultiparous	20	29.4	100.0
	Total	68	100.0	
		Number	Percentage	Cumulative percentage
BMI	<5 years	28	41.2	41.2
	5-10 years	18	26.5	67.6
	>10 years	22	32.4	100.0
	Total	68	100.0	
		Number	Percentage	Cumulative percentage
	Thin	1	1.5	1.5
	Normal	10	14.7	16.2
	Obese	57	83.8	100.0
	Total	68	100.0	

BMI: body mass index

In our study, patients underwent transvaginal ultrasonography, and the thickness of the endometrium was evaluated. The thickness values of the endometrium from the ultrasonography and the findings of endometrium cancer are given in Table 2.

In our study, 22.1% (n=15) of 68 patients were given hormone replacement treatment, while 77.9% (n=58) were not. The 6 patients in our study that were diagnosed with endometrial cancer did not receive hormone replacement treatment. Of the patients, 29.4% (n=20) smoked, and 2 of these patients were diagnosed with endometrial cancer. The rate of non-smokers (n=48) was 70.6%, and 4 of these patients were diagnosed with endometrial cancer. Of 68 patients, only one used alcohol. In terms of systematical diseases, 17 patients had diabetes mellitus (DM), and 2 of these patients had endometrial cancer. Twenty-two patients had hypertension (HT), and 4 of these patients had endometrial cancer. The coexistence of DM and HT was observed in 2 of 6 patients with endometrial cancer, and hypothyroidism was observed in 2 patients.

The patients included in the study underwent transvaginal ultrasonography. The thickness of the endometrium, uterine polyp, myoma, hyperplasia, and cancer findings were investigated. The results were compared with those of patients diagnosed with endometrial cancer (Table 3).

A statistically significant difference was detected between the diagnosis of endometrial cancer and the thickness of the endometrium. In 6 patients diagnosed with endometrial cancer, the thickness of the endometrium was greater than 5 mm ($p<0.05$).

No cancer was observed in any of the patients whose ultrasonographic examination results were reported to be normal. Histo-

pathological evaluation revealed cancer in 2 patients who had previously been diagnosed with endometrial polyp. Cancer was not observed in patients with hyperplasia and myoma.

All 68 patients included in the study underwent cervical smear tests under appropriate conditions. The results of the smear tests are shown in Table 4.

The smear test results were normal in 62 patients. The test revealed HSIL in 3 patients, atypical squamous cells of undetermined significance (ASC-US) in 1 patient, AGC-US in 1 patient, and ASC-H in 1 patient. In 6 patients diagnosed with endometrial cancer, the results of the smear test were found to be normal, and no significant relationship was detected between diagnosis of endometrial cancer and the smear results.

Endometrial biopsies were performed for all patients in the study. The results are presented in Table 5.

Of the 68 patients, 41.2% (n=28) had atrophic findings and 35.3% (n=24) had polyp. Hyperplasia was found in 5 patients. Endometrial cancer was detected in 8.8% (n=6) of patients, and cervical cancer was found in 2.9% (n=2).

DISCUSSION

Postmenopausal bleeding is an important finding requiring differential diagnosis in cervical and endometrial diseases. Although there are obvious clinical methods for the diagnosis and scanning of cervical pathologies, no scanning method is available for endometrial pathologies. The incidence of endometrial carcinoma in women with postmenopausal bleeding was reported to be between 3.9% and 17.9% in previous stud-

Table 2. Endometrial thickness and endometrial cancer findings in transvaginal ultrasonography

			Endometrial cancer		Total
			+	-	+
EMC	<5	Number	0	23	23
		Expected value	2.0	21.0	23.0
		According to the thickness of EM	.0%	100.0%	100.0%
		According to the presence of cancer	.0%	37.1%	33.8%
		According to total	.0%	33.8%	33.8%
	>5	Number	6	39	45
		Expected value	4.0	41.0	45.0
		According to the thickness of EM	13.3%	86.7%	100.0%
		According to the presence of cancer	100.0%	62.9%	66.2%
		According to total	8.8%	57.4%	66.2%
Total		Number	6	62	68
		Expected value	6.0	62.0	68.0
		According to the thickness of EM	8.8%	91.2%	100.0%
		According to the presence of cancer	100.0%	100.0%	100.0%
		According to total	8.8%	91.2%	100.0%

EM: endometrium; EMC: Endometrial cancer

Table 3. Transvaginal ultrasonography findings and Endometrial cancer

			Endometrial cancer		Total
			+	-	+
USG	Normal	Number	0	34	34
		According to USG result	0%	100.0%	100.0%
		According to the presence of cancer	0%	54.8%	50.0%
	Polyp	Number	2	19	21
		According to USG result	9.5%	90.5%	100.0%
		According to the presence of cancer	33.3%	30.6%	30.9%
	Submucous myoma	Number	0	7	7
		According to USG result	0%	100.0%	100.0%
		According to the presence of cancer	0%	11.3%	10.3%
	Intramural myoma	Number	0	1	1
		According to USG result	0%	100.0%	100.0%
		According to the presence of cancer	0%	1.6%	1.5%
	Hyperplasia	Number	0	1	1
		According to USG result	0%	100.0%	100.0%
		According to the presence of cancer	0%	1.6%	1.5%
	Cancer	Number	4	0	4
		According to USG result	100.0%	0%	100.0%
		According to the presence of cancer	66.7%	0%	5.9%
	Total	Number	6	62	68
		According to USG result	8.8%	91.2%	100.0%
		According to the presence of cancer	100.0%	100.0 %	100.0%

USG: ultrasonography

Table 4. Smear results

		Number	Percentage	Cumulative percentage
Smear result	Normal	62	91.2	88.2
	HSIL	3	4.4	95.6
	ASC-US	1	1.5	97.1
	AGC-US	1	1.5	98.5
	ASC-H	1	1.5	100.0
	Total	68	100.0	

ASC-US: atypical squamous cells of undetermined significance; AGC-US: atypical glandular cells; HSIL: high-grade squamous intraepithelial lesion; ASC-H: atypical squamous cells—cannot exclude high-grade squamous intraepithelial lesion

ies (1, 2). This incidence was found to be 8.8% in our study. In our study, the rates of other causes of postmenopausal bleeding were 41.2% for atrophy, 7.4% for hyperplasia, 35.3% for polyp, 2.9% for submucous myoma, 2.9% for cervical cancer, and 1.5% for CIN-2. In the literature, atrophic endometrium is seen to be the most common pathology (60% to 80%) causing postmenopausal bleeding (3). In our study, the rate of atrophy

was found to be lower. The rates of other endometrial pathologies were higher.

D&C, which is a common endometrial sampling technique, is the most frequently used diagnostic method in patients with postmenopausal bleeding. In some small series of cases, patients underwent D&C immediately before hysterectomy, and pathologi-

Table 5. Endometrial biopsy results

		Number	Percentage	Cumulative percentage
Endometrial biopsy result	Atrophic	28	41.2	41.2
	Polyp	24	35.3	76.5
	Submucous myoma	2	2.9	79.4
	Hyperplasia	5	7.4	86.8
	Endometrial cancer	6	8.8	95.6
	Cervical cancer	2	2.9	98.5
	CIN-2	1	1.5	100.0
	Total	68	100.0	

CIN-2: cervical intraepithelial neoplasia

cal examination of the hysterectomy material revealed that 10% of endometrial lesions could not be detected by D&C (4). In the study by Epstein et al. (1), a diagnosis could not be established by D&C at the rate of 58% for polyps, 60% for atypical hyperplasia cases, and 11% for endometrial carcinomas. Many studies similar to those mentioned above suggest that D&C and other sampling techniques for the endometrium are not sufficient for the evaluation of patients with postmenopausal bleeding.

For the last decade, transvaginal ultrasonography has been widely used as an alternative method for the determination of at-risk patients for endometrial disease. In various studies, normal and abnormal thicknesses of the endometrium have been investigated through transvaginal ultrasonography in postmenopausal women. For the thickness of the endometrium, while some researchers accept cutoff values of 5 mm or less as normal, some accept values of 4 mm or less to be normal. However, some researchers have stated that regardless of the thickness of the endometrium, endometrial biopsy must definitely be performed for all patients with postmenopausal bleeding (5). In our study, endometrial polyp was found in 4 patients with endometrial thicknesses less than 5 mm. The detection of polyp in patients with endometrial thicknesses less than 5 mm suggests that the evaluation of endometrial thickness, endometrial morphology, and endomyometrial junction must be used in combination. Sheikh et al. (6) reported that even when the endometrial thickness was normal in patients with increased focal echogenicity, increased diffuse homogeneity, and irregular endometrial margins, it was necessary to perform an endometrial biopsy for these patients. The thickness of the endometrium was found to be 11 mm in one of 6 patients with endometrial cancer and greater than 20 mm in another 5 patients. Granberg et al. (7) found no endometrial cancer in any patients with endometrial thicknesses less than 8 mm among 205 women with postmenopausal bleeding. They reported the mean endometrial thickness as 18.2 ± 6.2 mm in patients diagnosed with endometrial cancer and as 3.4 ± 1.2 mm in patients with atrophic endometrium. They stated that if the cutoff value had been taken as 5 mm in that study, 70% of patients would not have undergone curettage. In the study conducted by Smith-Bindman et al. (8), various endometrial thicknesses were taken as cutoff values. According to this study, when the cutoff value was ac-

cepted as 2 mm or less, the sensitivity was 100%; however, the specificity was 38%. It was demonstrated that the sensitivity decreased but the specificity increased when the cutoff value was increased. TV-USG is considered to be a good auxiliary diagnosis and scanning method for revealing the etiology of bleeding in patients with postmenopausal bleeding.

CONCLUSION

Transvaginal ultrasonography must be the first diagnostic imaging technique applied to patients admitted due to the complaint of postmenopausal bleeding. While performing transvaginal ultrasonography, not only the endometrial thickness but also the endometrial morphology and endomyometrial junction must be carefully examined. Our study has revealed that the possibility of endometrial pathology (particularly endometrial cancer) is low when the endometrial thickness, which is measured through TV-USG, is 5 mm or less. If the endometrial thickness is greater than 5 mm, endometrial pathology is possible and endometrial curettage is necessary. Endometrial curettage is the gold standard in cases of postmenopausal bleeding.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Gaziosmanpaşa Taksim Training and Research Hospital.

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

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