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Retrospective examination of endometrial sampling results in women with abnormal uterine bleeding

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Abstract

Background: Abnormal uterine bleeding (AUB) is among the most significant and frequent causes of admission to the gynecology outpatient clinic. AUBs may manifest as the earliest sign of endometrial cancer. For the early detection and treatment of endometrial cancer, careful examination of AUBs is crucial.

Aim: The study was conducted to retrospectively evaluate the histopathological results of probe curettage materials applied to women who applied to the gynecology clinic for AUB and were hospitalized with the complaint of AUB.

Material and Methods: In the retrospective study planned between 2020 and 2021, all endometrial biopsies from 638 women with AUB reported to the gynecology clinic were reviewed and analyzed. The data were obtained from the archives of our hospital's gynecology and obstetrics clinic and pathology clinic.

Results: 638 cases were analyzed. The mean age of the patients was 47.94±9.53 years. Malignant pathology was detected in 20 cases (3.13%). Nineteen of these cases were seen in postmenopausal women. The most common pathology was found to be benign polyps at a rate of 19.91%. It was the most common benign pathology in women pre- and postmenopausal. Adenocarcinoma was detected in 13 (2.03%) postmenopausal cases while in only 1 (0.16%) of the premenopausal women.

Conclusion: Since more malignant pathologies are observed in postmenopausal women, women with asymptomatic or AUB complaints should be carefully monitored, and endometrial evaluation should not be skipped. Endometrial biopsies are valuable in the early detection of pre-cancerous and cancerous endometrial lesions, especially in postmenopausal women.

Key words: endometrial cancer, abnormal uterine bleeding, endometrial carcinoma

Introduction

One of the most important and common reasons for admission to the gynecology outpatient clinic is abnormal uterine bleeding (AUB) [1,2]. AUB reduces the quality of life by imposing unorthodox physical, emotional, sexual, social, and financial responsibilities on women [3]. AUB is abnormal changes in time, frequency, and volume patterns in blood flow in the menstrual cycle [3]. AUBs are shared among the reasons women apply to gynecology outpatient clinics in the pre and post-menopausal period during reproductive age. Approximately one out of every three applications is due to AUB [3]. The prevalence and prevalence of 10-30% in women of reproductive age led researchers to a common terminology for defining and classifying AUBs [2]. This standard classification was made by The International Federation of Gynecology and Obstetrics (FIGO) in 2011. This classification is named PALM-COEIN by FIGO [2–4]. In this classification, PALM is classified as a polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia; and the coin is classified as coagulopathy, ovulatory dysfunction, endometrial

causes, iatrogenic and not yet classified [4]. Although a common terminology has been acquired for healthcare professionals in the AUB after this classification, it is of great importance how reproductive women perceive abnormal uterine bleeding, with which complaints they come to the clinic, and in what period they come [2].

AUBs are often the first symptom of endometrial cancer. Endometrial cancer is the most common gynecological malignant tumor in developed countries and ranks second after cervical cancer in developing countries [5]. Careful evaluation of AUBs is of great importance for early diagnosis and treatment of endometrial cancer. Especially in the pre and post-menopausal period, women who apply with the complaint of AUB should be carefully evaluated [6].

Diagnosis is made by probe curettage in AUBs. After the probing process, a diagnosis is made according to the PALM-COEIN classification, and the follow-up and treatment process begins. Age, body mass index (BMI), and systemic diseases [such as diabetes and hypertension] of the patients pose a risk in terms of the malignancy potential of polyps. In addition, a relationship was found between menopausal status, hormonal replacement therapy, history of breast cancer, tamoxifen use, and development of malignancy from polyp [7–9]. Although many factors affect the diagnosis, the fact that the woman is in the post or premenopausal period increases both the rate of malignancy and the likelihood of developing endometrial cancer. When the literature is examined, it is seen that the malignancy rates of women in the premenopausal period who apply with the complaint of AUB are 0.4%. In comparison, the malignancy rates of women in the postmenopausal period are 7%. In particular, it is seen that experiencing AUB after menopause has a 17.5-fold effect on the malignant outcome rate.

Similarly, as a result of the diagnosis in the literature, it was found that the incidence of hyperplasia was 2.5 times higher in the postmenopausal group than in the premenopausal group, the incidence of the endometrial polyp was four times higher, the incidence of proliferative endometrium was 0.38 times lower, and 50% of women in the postmenopausal period were diagnosed with secretory endometrium [3,10]. In line with these results, timely AUB screening is essential in both endometrial cancer and eliminating women's complaints. The results of probe curettage performed due to AUB in clinics reveal the severity of the condition [2,3,7,10].

Our study aims to retrospectively evaluate the histopathological results of probe curettage materials applied to women who applied to the clinic due to AUB and were hospitalized with the complaint of AUB.

Material and methods

The data of 638 patients admitted to the Obstetrics and Gynecology Clinic of Karabük University Training and Research Hospital between 2020 and 2021 or hospitalized in the puerperal ward due to abnormal vaginal bleeding were retrospectively analyzed. Age, the premenopausal and postmenopausal status of 638 patients, histopathological results of the unit sending for biopsy, and probe curettage materials were recorded. Histopathological results were classified into four groups: benign, premalignant, malignant pathology, and inadequate sample.

Inclusion criteria: applying to the clinic due to abnormal uterine bleeding, being in the menopausal period.

Exclusion criteria: not being in the menopausal period, insufficient material received.

Data analysis

Statistical analysis of the study was performed with SPSS 20 computer software (SPSS, Chicago, United States). Since the Skewness and Kurtosis values of the data remained within the +2.0/-2.0 limit range, it was seen that the data showed normal distribution [11]. Chi-square [$\chi 2$] test was performed to compare categorical characteristics. Frequency, Percentage, Average, and Standard deviation of descriptive statistical methods were used to evaluate the study data. One-Way ANOVA was used in all three and above comparisons in the study. Bonferroni-corrected Tukey HSD comparison was performed to determine which group caused the difference in evaluating the significant difference in the groups. The data were evaluated at a 95% confidence interval and $p<0.05$ significance level.

Results

The data of 638 patients who underwent probe curettage due to abnormal vaginal bleeding in the clinic between 2020 and 2021 were evaluated. The results evaluated were divided into premenopausal and postmenopausal periods and analyzed. The mean age of the women included in the study was 47.94 ±9.53. It was observed that 46.9% (n=299) of the women were in the premenopausal period, and 53.1% (n=339) were in the postmenopausal period. When the units where the pathologies were taken were evaluated, it was seen that 35.3% (n=225) were in the puerperal-perinatology service, and 64.7% (n=413) were in the obstetrics and gynecology outpatient clinic (Table 1).

Table 1 Characteristics of the data included in the study

Features		Mean±Ss	Min-Max (Median)
Age		47,94±9,53	24- 87 (47)
		n	%
Menopause Status	Premenopausal Period	299	46,9
	Postmenopausal Period	339	53,1
Unit where pathology was taken	Postpartum-Perinatology Service	225	35,3
	Obstetrics qnd Gynecology Polyclinic	413	64,7
Total		638	100,0

According to the histopathological findings of the patients due to ASF, 78.4% (n=500) were benign, 3.1% (n=20) were malignant, 3.0% (n=19) were premalignant, and 15.5% (n=99) were insufficient. Pathology results according to benign, premalignant, and malignant lesion types are given in Table 2 as percentages and frequency.

The distribution of pathology results by sending unit is given in Table 3. There was a difference between the distribution of pathology results of the patients hospitalized in the Postpartum-Perinatology department compared to the patients admitted to the outpatient clinic ($p <0.05$) (Table 3).

The relationship between age distribution and pathology result distribution of the patients was explained by One-Way Analysis of Variance (ANOVA). According to the analysis results, a significant difference was found between the patient's age distribution and pathology result distribution ($p<0.05$). Between which groups these differences were determined by the Tukey test in post-hoc analysis [homogeneity of variances $p= 0.000$; $P<0.05$) (Table 4). According to the analysis results, pathology results show that the mean age of patients with benign malignancies is lower than those with malignancies and inadequacies. In comparison, the mean age of patients with malignancies is higher. These differences were also statistically significant ($p<0.05$).

Table 2 Histopathological findings of the data included in the study

Features		Mean±Ss	Min-Max (Median)
		n	%
General Histopathological findings	Benign	500	78,4
	Premalignant	19	3,0
	malignant	20	3,1
	Insufficient Sample	99	15,5
Characteristics of Histopathological Findings			
Benign Pathologies	Bening	145	22,7
	Bening, Atrophic Endometritis	2	0,3
	Bening, Irregular Proliferation	56	8,8
	Bening, Irregular Secretory endometrium	1	0,2
	Bening Polyp	127	19,9
	Bening, Proliferative Endometritis	51	8
	Bening Polyphosis Development	47	7,4
	Bening, Proliferative Polyp	2	0,3
	Bening, Secretory endometrium	69	10,82
Premaling Pathologies	Premaling, Atypical Secretory Endometritis	1	0,2
	Premalingn Simple hyperplasia without atypia	15	2,4
	Premaling Complex Atypia	3	0,5
Malignant Pathologies	Malignant Endometrioid Adenocarcinoma	14	2,2
	Maling Bercan Carcinoma	2	0,3
	Maling Endometrial Neoplasia	2	0,3
	Maling Carcinoma	2	0,3
	Insufficient Sample	99	15.5
Total		638	100,0

Pathology results according to the menopausal period of women are given in Table 5. According to the analysis results, it was found that the pathology results of women who had AUB in the postmenopausal period were higher than those who had AUB in the premenopausal period (Table 5). When the malignant pathology results were examined, it was found in 1 (5%) case in the premenopausal group and 19 (95%) cases in the postmenopausal group (Table 5).

The histological pathology distributions of the cases according to their menopausal status are given in Table 6. No comparison was made in the analysis results, and only which pathology was seen in which period was examined. In line with these results, the most common result in both pre and postmenopausal women was found to be benign pathology. In addition to these findings, more malignant pathologies were found in postmenopausal women. He incidence of adenocarcinoma in postmenopausal women was 13 times higher than in premenopausal women (Table 6).

Discussion

Abnormal uterine bleeding is the most common reproductive age problem in women [8]. AUB should be evaluated quickly and carefully for endometrial cancer in women older than 40 years of age, especially in postmenopausal women. One-third of outpatient visits to the gynecology and obstetrics outpatient clinic and more than 70% of the patients are AUB [8]. It is seen that OCD increases with age and is effective in the transformation of age into a risky condition, especially endometrial cancer [3,6,8,12]. In the study by Şahin et al., in order to compare the endometrial thickness and histopathological results measured by transvaginal ultrasonography in premenopausal patients with abnormal uterine bleeding, it was observed that the mean age of women was 40 years and above, and they were in the premenopausal period [6]. Aker et al. examined the endometrial results in women with abnormal uterine bleeding, and in their study involving 765 cases, it was observed that the mean age of women was 43.14±7.92 in the premenopausal group and 60.7±7.88 in the postmenopausal group [3].

Table 3 Distribution of pathology results according to the unit that sent the biopsy

	Benign n (%)	Permalignantn (%)	Malignant n (%)	Insufficientn (%)	Total n (%)*	p
Obstetrics and Gynecology Clinic	313(%75.8)	13(%3.1)	9(%2.2)	78(%18.9)	413(%100)	0.004
Postpartum-Perinatology service	187(%83.1)	6(%2.7)	11(%9.3)	21(%9.3)	225(%100)	
Total	500(%78.4)	19(%3.0)	20(%3.1)	99(%15.5)	638(%100.0)	

* Row percentage is taken. χ^2=13.08 Sd=3

Table 4 ANOVA results regarding the significance of the difference between age and pathology outcome distributions

Pathology outcome distributions		n	x̄	ss	F	P	Difference between groups
Patient age	(1) Benign	500	46.76	8.383	18.423	0.000	1<3 p=0.000
							1<4 p=0.005
	(2) Permalign	19	50.00	12.529			2 <3 P=0.031
	(3) Malignant	20	60.05	8.500			3>1 p=0.000
	(4) Insufficient	99	51.02	11.930			3>2 p=0.031
							3>4 p=0.002
							4>1 p=0.005
							4<3 p=0.002
Homogeneity of variances = 0.000							

Table 5 Pathology results by menopausal period

Menopause Status	Benin		permaligin		malignant		Insufficient		Test Statistic*	p
	n	%	n	%	n	%	n	%	28,755	0,00
Premenopausal	259	51,8	8	42,1	1	5,0	31	31,3		
Postmenopausal	241	48,2	11	57,9	19	95,0	68	68,7		

*chisquare

Table 6 Histopathological findings of the cases according to their menopausal status*

Characteristics of Histopathological Findings	Menopoz Durumu					
	Premenopause Period			Postmenopause Period		
	n	Satır%	Sütun %	n	Satır%	Sütun %
Bening	69	47,59	23,1	76	52,41	22,4
Bening, Atrophic Endometritis	0	0,00	0,00	2	100,00	0,6
Bening, Irregular Proliferation	24	42,86	8,8	32	57,14	9,4
Bening, Irregular Secretory endometrium	1	100,00	0,3	0	0,00	0,00
Bening Polyp	61	48,03	20,4	66	51,97	19,5
Bening, Proliferative Endometritis	31	60,78	10,4	20	39,22	5,9
Bening Polyphosis Development	19	40,43	6,4	28	59,57	8,3
Bening, Proliferative Polyp	2	100,00	0,7	0	0,00	0,00
Bening, Secretory endometrium	52	75,36	17,4	17	24,64	5,0
Premaling, Atypical Secretory Endometritis	1	100,00	0,30	0	0,00	0,00
Premalingn Simple hyperplasia without atypia	7	46,67	2,30	8	53,33	2,40
Premaling Complex Atypia	0	0,00	0,00	3	100,00	0,90
Malignant Endometrioid Adenocarcinoma	1	7,14	0,30	13	92,86	3,80
Maling Bercan Carcinoma	0	0,00	0,00	2	100,00	0,60
Maling Endometrial Neoplasia	0	0,00	0,00	2	100,00	0,60
Maling Carcinoma	0	0,00	0,00	2	100,00	0,60
Insufficient Sample	31	31,31	10,4	68	68,69	20,1

*Comparison analysis was not performed in the table, only the histopathological findings between groups were examined.

In a retrospective study by Çelik and Güngör involving 705 cases, it was observed that the mean age of women was 46.93±9.04 years [12]. n our study, it was observed that the mean age of the women who came with the complaint of AUB was 47.94±9.53 years, 46.9% in the premenopausal period, and 53.1% in the postmenopausal period. These findings are similar to the average age of women with the complaint of AUB in the literature [3,6,12].

AUB is among the early symptoms of endometrial cancer. Women presenting with OCD anywhere in the premenopausal or postmenopausal period should be closely evaluated for cancer incidence [6,13–15]. When the literature was examined, it was seen that women who came with the complaint of AUB were diagnosed with endometrial cancer in the range of 6.2-15.2% [10,15–18]. In the studies in our country, this rate was found to be between 0.3-5% [3,6,12]. Bosch et al. investigated different endometrial and other intracavitary pathologies in women who presented with abnormal uterine bleeding using the International Endometrial Tumor Analysis (IETA) terminology before and after menopause and found endometrial cancer in 137 (6.2%) of women in their study involving 2856 women [15]. In a prospective observational study by Saccardi et al. Investigating the clinical relationship between the endometrial thickness (ET) and abnormal uterine bleeding (AUB) on the risk of endometrial cancer [EC] in a cohort of postmenopausal patients undergoing diagnostic hysteroscopy and endometrial biopsy, 16 (15.2%) of 105 women with only complaints of AUB were diagnosed with an endometrium [17]. In the study of Şahin et al., it was observed that 0.3% (n=2) of the women who applied to the clinic with AUB were diagnosed with endometrial cancer [6]. In the study of Aker et al., it was found that 5% (n=12) of women who applied with AUB were diagnosed with endometrial cancer [3]. In the studies of Çelik and Güngör involving 705 women, endometrial cancer was found in 2.4% (n=17) and other types of carcinomas in 0.4% (n=4) [12]. In the study of Sufia et al., in which 6458 Saudi women who applied to the clinic with AUB hemorrhage in the last 13 years were examined, it was observed that 1.88% (n=122) of women were diagnosed with endometrium [18]. In our study, it was observed that 3.1% (n=20) of the women who applied to the clinic with AUB were diagnosed with malignancy, and this result is consistent with the literature. Endometrial cancer or malignant diagnosis in AUBs increases with increasing age and is more common in the postmenopausal period [18]. When the literature is examined, it is seen that women diagnosed with malignancy are in the postmenopausal period or over 50 years of age [3,12,16,18]. This result is consistent with the literature and in our study, 11 of 20 women diagnosed with malignancy were found to be in the postmenopausal period.

As the unmet effect of estrogen continues with age, changes in the endometrium cause an increase in endometrial glands, and this increase causes endometrial hyperplasia without simple atypia [12]. Our study observed hyperplasia without Premalingn Simple atypia in 15 cases. 46.67% (n=7) of these cases were seen in the premenopausal period and 53.33% (n=8) in the postmenopausal period. When the literature is examined, the incidence rates of hyperplasia without simple atypia differ [3,12,15,18]. In the study of Çelik and Güngör, hyperplasia without simple atypia was 66.7% under the age of fifty, while it was 33.3% in women aged fifty and over [12]. In the study of Aker et al., hyperplasia without simple atypia was observed in 32 (4.2%) cases, and only two were in the postmenopausal period [3]. In the study of Bosch et al., the rate of hyperplasia

without simple atypia was found to be 6.7% (n=148), 66.89% (n=99) of 148 women were in the premenopausal period, and 33.10% (n=49) were in the postmenopausal period [15]. In the study of Sufia et al., simple atypical hyperplasia was observed in 254 (3.9%) cases; 18 (2.6%9 of these cases were under 40 years of age, 152 [3.4%] were between 40-55 years of age, and 84 (6.5%) were over 55 years of age [18]. In our study, hyperplasia without simple atypia was observed more in the postmenopausal period. The reason for this is thought to be the difference in interpretation between simple atypical endometrial hyperplasia and endometrial polyp in the differential diagnosis.

Endometrial polyp is one of the common causes of AUB [18,19]. This rate varies between 8-18% in studies [3,12,15,18]. The endometrial polyp was 33% in the study of Aker et al.; 34.5% in the study of Çelik and Güngör; 9.5% in the study of Kucur et al.; 18.3% in the study of Sufi et al. and 34.6% in the study of Bosch et al. [3,12,15,18,20]. In our study, the polyp was detected in 20.22% of the cases.

Endometrial adenocarcinoma [endometrial cancer] is also encountered in women who apply to the clinic due to AUB. The most important clinical symptom of endometrial cancer, especially in postmenopausal women, should be monitored very carefully, and the follow-up of these women should not be missed. The probability of adenocarcinoma in women presenting to the clinic with the complaint of AUB varies between 0.5-5%. These rates were found to be higher in postmenopausal women [3,12,15,18,20]. n the study of Çelik and Güngör, the rate of adenocarcinoma was 2.4% (n=17), and 13 of these cases were observed in women aged 50 and over [12]. In the study of Kucur et al., adenocarcinoma was observed in 6 cases (0.8%), and 4 of these cases were found to present with bleeding complaints in the postmenopausal period [20]. In the study of Aker et al., malignant pathology was detected in 12 cases (5%), and 9 of these cases were in the postmenopausal period [3]. In the study of Sufi et al., adenocarcinoma was detected in 86 cases (1.88%), and it was observed to be between the ages of 37-80 [18]. In the study of Bosch et al., endometrial cancer was observed in 137 cases (4.79%), and 127 of these cases were found to be in the postmenopausal period [15]. In our study, adenocarcinoma was observed in 14 cases (4.19%), and 13 of these cases were found to be in the postmenopausal period. Our results are consistent with the literature and have shown that women in the postmenopausal period require careful clinical examination of OCD complaints.

Limitations of the study

Conducting the study in a single center and in a single province and including the data of the last two years constitute an important limitation. The results of the study may form a basis for further studies in the field of investigating the outcomes of patients suffering from abnormal uterine bleeding in Karabuk and elsewhere.

Conclusion

Our study showed that endometrial cancer or malignant pathology increased with age. Mainly, the presence of AUB in the postmenopausal period was found to be an important differential diagnosis for defining endometrial cancer. It is essential not to make an advanced differential diagnosis for endometrial cancer and to perform endometrial sampling in postmenopausal women experiencing AUB or metrorgy.

Ethical board approval

University Scientific Non-Interventional Clinical Research Ethics Committee (protocol date and number: 25.04.2022 and Number: E-77192459-050.99-123196 Decision No: 2022/896).

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