

Evaluation of Endometrial Histopathology of Patients Presenting with Abnormal Uterine Bleeding

Anormal Uterin Kanama ile Başvuran Hastaların Endometrial Histopatolojilerinin Değerlendirilmesi

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Özet

Amaç: Anormal uterin kanama jinekoloji polikliniğinde sık karşılaşılan önemli bir semptomdur. Çalışmamızda anormal uterin kanamaya sebep olan endometrial patolojilerin neler olduğunun tespit edilmesi amaçlanmıştır.

Gereç ve Yöntemler: Anormal uterin kanama şikayetiyle kliniğimize başvuran ve endometrial örnekleme yapılmış hastaların patoloji sonuçları retrospektif olarak incelenmiştir. Bulgular hastaların postmenopoz ve premenopozal dönemde olmalarına göre sınıflandırılmış ve karşılaştırılmıştır.

Bulgular: Çalışmaya toplam 878 hasta dahil edildi. Hastaların yaş ortalaması 47,59±7,91 yıl olarak tespit edildi. En sık gözlenen semptom menometroraji %58,1 idi. En sık saptanan patolojik bulgu hem premenopozal ve hem de menopozal hastalarda (%29,69 ve %24,31) endometrial polipti. Premalign ve malign lezyonların görülme sıklığı premenopozal hastalarda %2,7 ve postmenopozal hastalarda %8,25 olarak bulundu.

Sonuç: Anormal uterin kanama hem postmenopozal hem de premenopozal hastalarda malignensilerle ilişkili olabilir. Bu semptomla başvuran hastalarda endometrial örnekleme yapılması malign ve premalign lezyonların erken tanı ve tedavisinin sağlanmasında büyük önem taşımaktadır.

Anahtar kelimeler: Anormal uterin kanama, biyopsi, patoloji

Abstract

Objective: Abnormal uterine bleeding is an important symptom frequently encountered in the gynecology outpatient clinic. In our study, it was aimed to determine the endometrial pathologies that cause abnormal uterine bleeding.

Material and Methods: The pathology results of patients who applied to our clinic with the complaint of abnormal uterine bleeding and underwent endometrial sampling were retrospectively analyzed. Findings were classified and compared according to whether the patients were in the postmenopausal or premenopausal period.

Results: A total of 878 patients were included in the study. The mean age of the patients was 47.59±7.91/year. The most common symptom was menometrorrhagia 58.1%. The most common pathological finding was endometrial polyp in both premenopausal and postmenopausal patients (29.69% and 24.31%). The incidence of premalignant and malignant lesions was 2.7% in premenopausal patients and 8.25% in postmenopausal patients.

Conclusion: Abnormal uterine bleeding may be associated with malignancies in both postmenopausal and premenopausal patients. Performing endometrial sampling in patients presenting with this symptom is of great importance in providing early diagnosis and treatment of malignant and premalignant lesions.

Keywords: Abnormal uterine bleeding, biopsy, pathology

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INTRODUCTION

Abnormal uterine bleeding (AUB) is a complaint that many women face at some point in their lives. AUB constitutes almost one-third of the reasons women apply to the gynecology outpatient clinic (1). AUB is defined as disturbances in the amount, frequency, duration, or rhythm of menstrual bleeding (2). Its incidence has been determined as 10-30% in women of reproductive age (3) This symptom may appear as spotting, breakthrough bleeding, postmenopausal bleeding, or menometrorrhagia. This symptom, which presents in so many different ways, can also be associated with a wide range of diseases.

When the etiological factors are examined, it is seen that many different clinical conditions are encountered with AUB. AUB can be seen in almost all age groups as a sign of malignant lesions in the postmenopausal period from bleeding that occurs in female babies due to maternal hormones in the neonatal period. Traumas, hormonal disorders, coagulation systemic diseases, endometrial lesions, emotional effects, systemic diseases, and some malignancies may also present as AUB (4).

In this study, the histopathological results of patients who applied to the gynecology outpatient clinic with the complaint of AUB and underwent endometrial biopsy were reviewed retrospectively. Knowing the diseases that may be associated with these symptoms, which are frequently encountered in the gynecology outpatient clinic, plays a key role in determining the management of these patients. We think our study will improve the management of these cases by increasing the awareness of endometrial pathologies that occur with AUB.

MATERIALS AND METHODS

Patients who applied to the gynecology outpatient clinic with the complaint of irregular vaginal bleeding between January 2020 and July 2022 and who underwent endometrial biopsy were included in the study. The files of these patients were reviewed retrospectively. Patients were divided into two groups premenopausal and menopausal. The age of the patients and the distribution and frequency of their symptoms were determined. The histopathologic results and incidence of the patients in both groups were determined. Results reported as proliferative, glandular, or secretory endometrium were considered physiological findings. Results reported as simple endometrial hyperplasia with/without atypia, endometrial hyperplasia with/without complex atypia, endometrial intraepithelial neoplasia, and high-grade squamous intraepithelial lesion were considered premalignant. Age, additional disease sta-

tus, background, and ultrasound findings of malignant cases were also stated.

Statistical Analysis

Statistical analysis and ratios were performed using the SPSS 20.0 program. Kolmogorov Smirnov test was used to evaluate the distribution of the data. Parameters conforming to the normal distribution were compared with the Student t-test, and the parameters not conforming to the normal distribution were compared with the Mann-Whitney U test. Proportional comparisons were made with the chi-square test (Fisher's exact test). In the statistical evaluation, $p < 0.05$ was considered significant at the 95% confidence interval.

Our study was reviewed according to the "Helsinki Declaration" and "Good Clinical Practice Guideline" and was prepared "duly" according to the guideline. Ethics committee approval was granted by Recep Tayyip Erdogan University Non-interventional Clinical Research Ethics Committee (Decision no: 2023/07 date: 01/05/2023).

RESULTS

A total of 878 patients were included in the study. It was determined that 660 (75.2%) of the patients were in the premenopausal period and 218 (24.8%) were in the postmenopausal period. The mean ages of the patients in the premenopausal and postmenopausal periods were 45.05 ± 5.37 and 55.27 ± 9.3 , respectively (Mann Whitney U test $p < 0.001$). When the symptoms of the patients included in the study were examined, 530 (58.1%) patients had menometrorrhagia, 227 (25.9%) patients had postmenopausal bleeding, 75 (8.5%) had spots, 48 (5.5%) had menstrual irregularity, and 18 (2.1%) patient applied with the complaint of breakthrough bleeding. Demographic data of the data included in the study are shown in **Table 1**.

Premalignant or malignant lesions were detected in 15 (2.27%) premenopausal and 18 (8.25%) postmenopausal patients. The difference in the incidence of premalignant and malignant lesions between the two groups was statistically significant (chi-square test $p < 0.001$). When the distribution of histopathologic results of endometrial biopsies is examined, physiological findings 458 (52.16%), endometrial polyp 249 (28.35%), irregular proliferative endometrium 62 (7.06%), endometritis, cervicitis 59 (6.71%), atrophic endometrium 13 (1.48%), endometrial hyperplasia without simple atypia 12 (1.36%), endometrial cancer 9 (1.02%), endometrial hyperplasia with complex atypia 3 (0.34%), leiomyoma 3 (0.34%), squamous carcinoma 2 (0.22%),

Table 1. Demographic data of the data included in the study

Age/year mean±SD	47.59±7.91
Gravida mean±SD	2.87±1.36
Parite mean±SD	2.7±1.2
	n (%)
Menopause	218 (24,8)
Premenopausal	660 (75,2)
Symptom	
Menometrorrhagia	530 (58,1)
Postmenopausal bleeding	227 (25,9)
Spotting	75 (8,5)
Menstrual irregularity	48 (5,5)
Intermediate bleeding	18 (2,1)

SD: Standard deviation

endometrial intraepithelial neoplazi 2 (0.22%), high-grade squamous intraepithelial lesion 2 (0.22%), large cell neuroendocrine carcinoma 1 (0.11%), malignant mixed müllerian tumor (carcinosarcoma) 1 (0.11%), serous carcinoma 1 (0.11%), insufficient material 1 (0.11%) were detected. The distribution of endometrial biopsy results according to the menopausal status of the patients included in the study is shown in **Table 2**.

Ultrasound findings, symptoms, and additional diseases of malignant cases were examined. The patient, whose pathology was determined as serous carcinoma, was 60 years old, G5P3Y3A2, and had a postmenopausal bleeding complaint for two months. It was determined that she had diabetes, hypertension, and a history of endometrial cancer in her mother in her medical history. On ultrasound, the endometrium was 4 mm and irregular. One of the patients

Table 2. Distribution of Endometrial Biopsy Results in Menopausal and Premenopausal Patients

	Premenopausal n (%)	Menopause n (%)	Total n (%)
Physiological findings	345 (52.27)	113 (51.83)	458 (52.16)
Endometrial polyp	196 (29.69)	53 (24.31)	249 (28.35)
Irregular proliferative endometrium	53 (8.03)	9 (4.12)	62 (7.06)
Endometritis cervicitis	45 (6.81)	14 (6.42)	59 (6.71)
Atrophic endometrium	3 (0.45)	10 (4.58)	13 (1.48)
Simple endometrial hyperplasia without atypia	8 (1.21)	4 (1.83)	12 (1.36)
Endometrial cancer	1 (0.15)	8 (3.66)	9 (1.02)
Endometrial hyperplasia with complex atypia	2 (0.3)	1 (0.45)	3 (0.34)
Leiomyoma	3 (0.45)	0 (0)	3 (0.34)
Squamous carcinoma	0 (0)	2	2 (0.22)
Endometrial intraepithelial neoplasia	2 (0.3)	0 (0)	2 (0.22)
High Grade Squamous intraepithelial lesion	1 (0.15)	1 (0.45)	2 (0.22)
Large cell neuroendocrine carcinoma	1 (0.15)	0 (0)	1 (0.11)
Malignant mixed müllerian tumor (Carcinosarcoma)	0 (0)	1 (0.45)	1 (0.11)
Serous carcinoma	0 (0)	1 (0.45)	1 (0.11)
Insufficient material	0 (0)	1 (0.45)	1 (0.11)
Total	660 (100)	218 (100)	878 (100)

with squamous carcinoma, a 49-year-old G3P3Y3, had a postmenopausal bleeding complaint for twenty days. The ultrasound was unremarkable. As a result of the smear, she was HPV type 16 positive and had a goiter operation cluster. The other patient was 72 years old and presented with complaints of g4p4y4 weight loss and postmenopausal bleeding. Ultrasound revealed 8 mm irregular and fundal 5 cm fibroids in the endometrium. In her history, it was learned that she had hypertension her mother had breast cancer, her daughter had cervical cancer and her sister had bowel cancer. A 60-year-old nulliparous patient with a malignant mixed müllerian tumor (Carcinosarcoma) was admitted with the complaint of falling pieces. On ultrasound, a 9 cm mass image that could not be distinguished from the uterine border was observed in the endometrial cavity. There were no features on his resume. A 57-year-old G3P3Y3 patient with large cell neuroendocrine carcinoma was admitted with the complaint of postmenopausal bleeding. On ultrasound, the endometrium was detected as 10 mm irregular. He had a history of heart failure, kidney failure, and diabetes mellitus.

When the endometrial cancer cases were examined, 1 case consisted of premenopausal and 8 cases consisted of postmenopausal patients. Four of the postmenopausal cases had a history of hypertension and diabetes mellitus. The premenopausal patient was 43 years old, nulliparous, and had one kidney.

DISCUSSION

Abnormal uterine bleeding is a very common symptom in women. It has been suggested to use the PALM-COEIN classification for the classification of etiological factors (4). PALM-COEIN; It is an acrostic word formed from the initials of the words polyp, adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial pathologies, iatrogenic, and unclassifiable. As stated in this classification, this symptom may also be associated with malignancies. For this reason, it needs to be carefully evaluated. Pregnancy should be ruled out first in a patient presenting with this complaint. Then, it should be started to investigate the etiological factors with further examinations and examinations.

In our study, the most common histopathologic diagnosis in patients presenting with AUB was the glandular, proliferative, and secretory endometrium, which are accepted as benign physiological findings. In a study conducted in our country on this subject, it was determined that physiological findings were the most

common diagnosis (1). In these patients, other than endometrial cavity pathologies, diseases that may cause AUB should be investigated. The findings in our study are compatible with the literature.

Endometrial polyps are tissue masses that grow into the endometrial cavity as a result of hyperplasia of the endometrial gland and stroma. In studies conducted in our country, the frequency of endometrial polyps was found to be 23.7% (5). In another study, the frequency of endometrial polyps was reported as 45, 9% (6). It is a benign lesion, and in our study, it appeared as the most common endometrial pathology causing AUB. Our findings are compatible with the literature.

Vaginal and endometrial infections can also be encountered with AUB. In various studies, the frequency of endometritis was reported as 4.6% in patients presenting with the complaint of AUB (7). In our study, the frequency of endometrial/cervicitis was found to be 6.71%, which is consistent with the literature.

In the normal cycle of the menstrual cycle, the endometrium under the influence of estrogen thickens. Afterward, this layer matures with the effect of progesterone. If the endometrium under the influence of estrogen does not meet with enough progesterone, endometrial hyperplasia occurs. It is called unopposed estrogen. All of these endometrial lesions, classified as simple with/without atypia or complex with/without atypia, are considered precancerous. In a study, the frequency of endometrial hyperplasia was reported as 9.2% (8). In another study, the frequency of endometrial hyperplasia was reported to be 10% (10%) in premenopausal patients who underwent endometrial biopsy with the complaint of AUB, and 6% in menopausal patients (9). In another study conducted in our country, the frequency of endometrial hyperplasia was reported as (3.6%) (6). In our study, the frequency of endometrial hyperplasia was found to be lower.

Endometrial cancer is the most common gynecological cancer. The most common symptom is postmenopausal bleeding (10). The frequency of endometrial cancer was reported as 1.8% in a study (11). In another study, it was reported as 3.8% (12). In our study, our findings were consistent with the literature, and the frequency of endometrial cancer was found to be 1.02.

When the risk factors of endometrial cancers are examined, the presence of diabetes mellitus and obesity are encountered. In our study, four of 9 patients with endometrial cancer had a history of diabetes mellitus. In other malignant cases, the presence of diabetes and a family history of cancer are noteworthy. In addition, an increase in endometrial thickness or irregular

appearance of the endometrial cavity on ultrasound examination is another remarkable finding. Also, as expected, malignancy is common in postmenopausal patients.

Conclusively, abnormal uterine bleeding is a fairly common symptom. This symptom needs careful investigation. Especially in patients with a history of diabetes mellitus in the postmenopausal period or a family history of cancer, malignancies should be considered. In the management of patients presenting with this symptom, performing endometrial sampling after excluding pregnancy may provide early diagnosis of possible malignancies. In addition, the detection and treatment of non-malignant diseases will be possible with endometrial biopsy.

Ethical Approval: Ethical approval was granted by Recep Tayyip Erdogan University Ethics Committee (Decision no: 2023/07 date: 01/05/2023). Our study was reviewed according to the “Helsinki Declaration” and “Good Clinical Practice Guideline” and was prepared “duly” according to the guideline.

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