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Importance of endometrial biopsy in premenopausal women without risk factors for endometrial cancer

Endometriyum kanseri için risk faktörü olmayan premenopozal kadınlarda endometriyal biyopsinin önemi

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ÖZ

Amaç: Anormal uterin kanaması olan kadınlarda endometrial biyopsi için uygun yaş tartışmalıdır. Bu çalışmada endometriyum kanser için risk faktörü olmayan ve menorajisi olan 40-49 yaş arası premenopozal kadınlarda endometriyal biyopsi sonuçlarını değerlendirmeyi amaçladık.

Gereçler ve Yöntem: 1 Ocak 2017-30 Haziran 2021 tarihleri arasında hastanemizin Kadın Hastalıkları ve Doğum kliniğinde diagnostik amaçlı endometrial biyopsi yapılan hastaların kayıtları retrospektif olarak incelendi. Bu hastalardan endometrial biyopsi sonuçları olan menorajili 40-49 yaş arası premenopozal kadınlar çalışmaya dahil edildi. Risk faktörü olan hastalar çalışma dışı bırakıldı.

Bulgular: Çalışmaya, menorajisi olan 176 premenopozal hasta dahil edildi. Risk faktörleri olmayan hastaların biyopsi sonuçlarında malignite saptanmadı. Toplam 6 olguda endometrial hiperplazi (EH) (%3.4) saptandı. EH saptanan olguların 1'i (%0.6) atipili hiperplazi, 5'i (%2.8) atipisiz hiperplazi olarak saptandı.

Sonuç: Risk faktörü olmayan anormal uterin kanama ile başvuran 40-49 yaş grubu premenapozal hastalarda endometrial biyopsi rutin değildir ve seçilmiş hastalarda uygulanmalıdır.

Anahtar Kelimeler: Endometrial biyopsi, endometrium kanseri, menoraji, risk faktörleri

ABSTRACT

Objective: In women with abnormal uterine bleeding, the appropriate age for endometrial biopsy remains controversial. In this study, we aimed to evaluate the results of endometrial biopsy in premenopausal women aged 40-49 years with menorrhagia and without risk factors for endometrial cancer.

Material and Methods: The records of patients who underwent endometrial biopsy for diagnostic purposes at the gynecology and obstetrics clinic of our hospital between January 1, 2017 and June 30, 2021 were retrospectively reviewed. Among these patients, premenopausal women aged 40-49 years with menorrhagia who had endometrial biopsy results were included in the study. Patients with risk factors were excluded from the study.

Results: A total of 176 premenopausal patients with menorrhagia were included in the study. According to the biopsy results of these patients without risk factors, no malignancy was detected. Endometrial hyperplasia was present in six patients (3.4%), of whom (0.6%) had hyperplasia with atypia and five (2.8%) had hyperplasia without atypia.

Conclusion: Endometrial biopsy is not routine in premenopausal patients aged 40-49 years who are admitted with abnormal uterine bleeding without risk factors and should be performed in selected patients.

Keywords: Endometrial biopsy, endometrial cancer, menorrhagia, risk factors

INTRODUCTION

Endometrial cancer (EC) is the most common gynecological cancer in developed countries and the second most common gynecological cancer after cervical cancer in developing countries (1). While its incidence is 8.3/100000 in the world, the lifetime risk of developing cancer is 1%. (2). Unopposed estrogen exposure is the most typical risk factor for EC. Other risk factors include advanced age, obesity, family history, tamoxifen use, polycystic ovary syndrome, anovulation, type 2 diabetes mellitus, nulliparity, early menarche, and late menopause (2). In patients with EC, the most common and suspicious symptom is abnormal uterine bleeding. Endometrial biopsy is a traditional method used for diagnostic purposes in patients presenting with abnormal uterine bleeding. In patients with suspected EC, endometrial biopsy can be performed as dilatation and curettage (D&C) or with the pipelle method, which is simpler, faster and cheaper (3,4).

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Most patients with EC are diagnosed at an early stage (80% in Stage 1), and more than 90% of cases are women aged 50 years and over (5). The incidence reaches the highest level over the age of 65 years. There is no screening method to reduce mortality in patients without risk factors. While EC may develop in some patients without a high risk, it may not develop in some with a high risk. Therefore, in this study, we aimed to evaluate the results of endometrial biopsy in premenopausal women aged 40-49 years with menorrhagia and without risk factors for EC.

MATERIALS AND METHODS

Study design and participants

In this study, the records of patients who underwent endometrial biopsy for diagnostic purposes at the gynecology and obstetrics clinic of our hospital between January 1, 2017 and June 30, 2021 were retrospectively reviewed. Premenopausal women aged 40-49 years with menorrhagia who had available biopsy results were included in the study. Local ethics committee approval was obtained for the study (ethics committee number: 2021/17-04). The following exclusion criteria were used: biopsies with incomplete records, those with pathology results evaluated as insufficient material, and presence of risk factors (family history, obesity, tamoxifen use, anovulation, nulliparity, early menarche and late menopause, polycystic ovary syndrome, and type 2 diabetes mellitus).

Data collection

Clinical data were obtained from the patient epicrisis and pathology reports screened through the hospital electronic database. The patients' age, parity, menopausal status, transvaginal ultrasonography findings, gynecological examination findings, and histopathological findings (endometrial biopsy results) were recorded. The endometrial pathology results were grouped as hyperplasia without atypia, hyperplasia with atypia, endometritis, endometrial polyp, proliferative endometrium, secretory endometrium, atrophic endometrium, and EC.

Statistical Analysis

Data were analyzed using Statistical Package Social Sciences (SPSS), version 22.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics for continuous variables were expressed as mean ± standard deviation, minimum and maximum values, and categorical variables as numbers and percentages. The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk tests) methods. Pearson's chi-square or Fisher's test was used to compare categorical variables. A P value of <0.05 was considered to be statistically significant in all analyses.

RESULTS

The study included a total of 176 premenopausal patients who underwent endometrial biopsy due to menorrhagia and had no risk factors for EC. The median age of the patients was 45 (42-49) years. The demographic and clinical characteristics of the patients are shown in Table 1.

Table1. Demographic characteristic of patients

Variables	n (%)
Age (years)	45 (42-49)
Age group	
40-44 years	82 (46.6%)
45-49 years	94 (53.4%)
Parity	
1	28 (15.9%)
>1	148 (84.1%)
Biopsy techniques	
Pipelle	149 (84.7%)
D&C	27 (15.3%)
Endometrial Thickness (mm)	9.0 ± 1.1
Histology	
Endometrial carcinoma	0
Endometrial hyperplasia	6 (3.4%)
Benign pathology	170 (96.6%)

Data are presented as mean ± standard deviation, median and 25-75 percentiles or n (%)

D&C: dilation and curettage

Endometrial biopsy was performed with the pipelle method in 84.7% (n = 149) of the patients and with the D&C method in 15.3% (n = 27). While 46.6% of the patients were in the 40-44 years group, 53.4% were aged 45-49 years. No malignancy was detected in any of the biopsy results of the patients without risk factors for ED. Endometrial hyperplasia (EH) was detected in a total of six patients (3.4%), of whom one (0.6%) had hyperplasia with atypia (simple) and five (2.8%) had hyperplasia without atypia (Tables 2 and 3).

Table2. Histopathological diagnosis of endometrial biopsy

Histopathological diagnosis	n (%)
Proliferative endometrium	82 (46.6%)
Secretory endometrium	58 (33.0%)
Endometritis	10 (5.7%)
Atrophic endometrium	1 (0.6%)
Endometrial polyp	19 (10.8%)
Hyperplasia without atypia	5 (2.8%)
Hyperplasia with atypia	
Simple	1 (0.6%)
Complex	0
Endometrial cancer	0

Table3. Histopathological diagnosis according to age group

Histopathological diagnosis	Age group		P-value
	40-44 years	45-49 years	
Proliferative endometrium	37 (45.1%)	45 (47.9%)	0.715
Secretory endometrium	28 (34.1%)	30 (31.9%)	0.753
Endometritis	6 (7.3%)	4 (4.3%)	0.381
Atrophic endometrium	0	1 (1.1%)	0.349
Endometrial polyp	9 (11.0%)	10 (10.6%)	0.943
Hyperplasia without atypia	2 (2.4%)	3 (3.2%)	0.764
Hyperplasia with atypia	0	1 (1.1%)	0.349
Endometrial cancer	0	0	N.S.

N.S.: indicates not significant

We found a higher rate of EH in the 45-49 years group compared to the 40-44 years group. The patient with hyperplasia with atypia had follow-up biopsy results that were found to be normal.

DISCUSSION

As a result of this study, we determined that the risk of neoplastic and preneoplastic diseases is minimal in premenopausal women aged 40-49 years with menorrhagia without risk factors. Hyperplasia with atypia was found in one (0.6%) patient who underwent endometrial biopsy, and hyperplasia without atypia was present in five (2.8%) cases, while the pathology results were benign in the remaining 170 (96.6%) cases.

EC is the most common cancer among gynecological cancers. Although the incidence varies between geographical regions, approximately 200,000 new cases are diagnosed each year (6). The most common symptom of EC is abnormal uterine bleeding, and EC should be excluded in the presence of abnormal uterine bleeding in postmenopausal bleeding and women aged over 40 years with risk factors. Approximately half of women with abnormal uterine bleeding complaints are in the 40-50 years group (7). The most common cause of abnormal uterine bleeding in this age group is a benign pathology. The incidence of endometrial pathology (EH/EC) in premenopausal women with abnormal uterine bleeding shows variations according to populations, ranging from 5% to 14% (8). This may be due to the differences in the populations studied in terms of high or low risk factors. In our study, a benign endometrial pathology was found in most women (96.6%). Therefore, we recommend more selective patient selection to exclude more important endometrial pathologies.

EC is frequently seen in the postmenopausal period and has a worse course with increasing age (9). On the other hand, 14% of EC cases are in the premenopausal period and 5% are under 40 years. Aker et al. examined 765 cases of abnormal uterine bleeding and found the malignancy rate to be 1.6% (n=12). In the same study, while the malignancy rate was 0.5% (n = 3) in the premenopausal period, it was found to be 4.5% (n = 9) in the postmenopausal period (10). In the United States, the mean age at which women are diagnosed with EC is reported to be 61 years. While 32.6% of patients with EC are diagnosed between the ages of 55-64 years and 22.6% are aged 65-74 years at the time of diagnosis (11). Many studies in the literature support the idea that age is an independent prognostic factor (12). According to the results of our study, there was no malignancy in any of the 176 patients who presented with premenopausal abnormal uterine bleeding, while EH was detected in only six of these patients. All of our patients were premenopausal women aged 40-49 years with no malignancy results, indicating that age is an effective parameter in the development of EC.

Biopsy, as an easy-to-apply procedure producing fast results, is one of the diagnostic methods frequently used by gynecologists (13). However, it can raise questions in terms of the appropriate use of resources. The following are the reasons for the widespread use of endometrial biopsy: the first is the exclusion of EC. The second is to detect intrauterine pathologies in a wide range of diseases from reproductive diseases to benign gynecological diseases (14). When the endometrial biopsy results are examined, it is observed that 80% are reported as benign (15). Sari et al., evaluating the results of patients who underwent endometrial biopsy due to abnormal uterine bleeding, found that the most common pathology result was proliferative endometrium (38.2%) (16). Similarly, Jetley et al. reported the most common pathology result as secretory endometrium at a rate of 32.4%, followed by proliferative endometrium (30.5%) (17). In our study, proliferative endometrium was found in 46.6% of the patients who underwent endometrial biopsy with no risk factors for EC, and secretory endometrium

was present in 33.0%. Based on these data, it can be concluded that the anxiety experienced by patients with gynecological symptoms and the concern of physicians related to a possible delay in the diagnosis of cancer can result in the widespread use of endometrial biopsy. Clinicians should be more selective when evaluating endometrial biopsy indications, especially in the group of patients with premenopausal menorrhagia without risk factors for EC.

There are certain limitations of the study. First, the number of cases meeting the inclusion criteria was limited. Second, the study was conducted in a single center. Third, it had a retrospective design. Therefore, there is a need for prospective studies involving multiple centers.

CONCLUSIONS

When used in the presence of right indications, endometrial biopsy can be the gold standard in obtaining important findings; however, it can have negative consequences in terms of complications and healthcare costs if used inaccurately and inappropriately. We recommend that endometrial biopsy be performed more selectively in premenopausal women aged 40-49 years with menorrhagia without risk factors of EC.

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